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The BULLETIN of the ASSOCIATION for the STUDY of

INTERNAL SECRETIONS

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ENDOCRINOLOGY

THE BULLETIN of the ASSOCIATION for the STUDY of

INTERNAL SECRETIONS

APRIL-JUNE, 1919

THE FUNCTION OF THE CHROMAPHIL TISSUES

I. Pearlman and Swale Vincent

(From the Physiological Laboratory, University of Manitoba, Winnipeg, Canada)

The theory that the chromaphil tissues (and especially the medulla of the adrenal bodies) maintain, or help to maintain, the normal tone of the blood-vessels and other sympathetically innervated structures, is now generally abandoned, if we may judge by the attitude adopted by the writers of recent text-books (15). It is also recognized that the medulla of the adrenal body is not essential to life, and that the reduction of the adrenin content of the blood to a minute fraction of the normal amount does not affect the health of an animal (16). Certain phases of this question have been dealt with in a recent article in this Journal (18).

These statements, however, do not exclude the possibility that the chromaphil tissues play a part in certain reactions which are initiated elsewhere, as, for example, in those which result from stimulations of nerves in laboratory experiments.

It has been known for a long time that the rise of blood-pressure brought about by stimulation of the peripheral end of the splanchnic nerve is not simple. The curve obtained suggests at once that there is more than one factor concerned in its production. We have not been able to find any reproduc-

tion of tracings obtained previously to the work of Elliott, so that it is difficult to ascertain what was the precise form of curve which was considered to be typical under normal or under different experimental conditions.

Johansson (13) found that in the dog the curve presents two summits, and it has since been found that the same is generally true in other animals also.

Lehndorff (14) also worked with dogs and came to the conclusion that the first rise is due to vaso-constriction in the splanchnic area, the "step" to a temporary dilation of the heart, and the second rise to increased force and frequency of the heart-beat accompanied by vaso-constriction in the somatic area.

Elliott (6), who investigated the subject in cats, stated that in animals recently admitted and still in a frightened condition, the typical splanchnic curve cannot be obtained. But he regarded the typical curve as something different from that obtained by previous workers in the case of dogs. According to this author a well marked characteristic of the pressure curve seen when the splanchnics are stimulated under good conditions in the cat, is that it rises rapidly for nine or ten seconds; then, without any check in the heart's rhythm, the curve is sharply cut down nearly to the level from which it came, whence it rises slowly again so long as the stimulus is continued. The drop, according to Elliott, is due to the liberation of adrenin into the blood, and he gives what seems to be very convincing evidence in favor of this view.

V. Anrep (1, 2) who used dogs for his experiments, reports that stimulation of the splanchnic nerve causes a rise of blood-pressure which occurs in two phases. The second phase is accompanied by constriction of peripheral blood-vessels (even after denervation) and by acceleration and increased tone and augmentation of the heart (also after denervation). The secondary rise and all the concomitant phenomena are due to the discharge of adrenin into the circulation, and are absent after extirpation of both adrenal bodies. Every rise of blood-pressure, brought about by the agency of the nervous system, involves the co-operation of the chemical mechanism represented by the adrenal bodies. The constriction of blood-vessels

in denervated limbs under splanchnic stimulation, which was regarded by Bayliss (3) as a local reaction to increased pressure, is interpreted by V. Anrep as due to the action of adrenin. The rise of blood-pressure in asphyxia is also looked upon by this author as being partly due to constriction of somatic vessels as a result of the action of adrenin upon them.

Gley and Quinquaud (7, 8, 9, 10) have recently thrown doubt upon the validity of these experiments. They think that ligature of the vessels of the adrenal bodies or extirpation of the organs in the dog involves damage to some of the splanchnic vaso-constrictor fibres and that this accounts for the alteration in the splanchnic blood-pressure curve. In the cat and the rabbit, according to these authors, such alteration does not occur. In these animals the nerves are not so intimately connected with the adrenal bodies.

These criticisms on the part of Gley and Quinquaud have prompted us to a re-investigation of the subject. We have performed a very large number of experiments upon dogs, cats and rabbits.

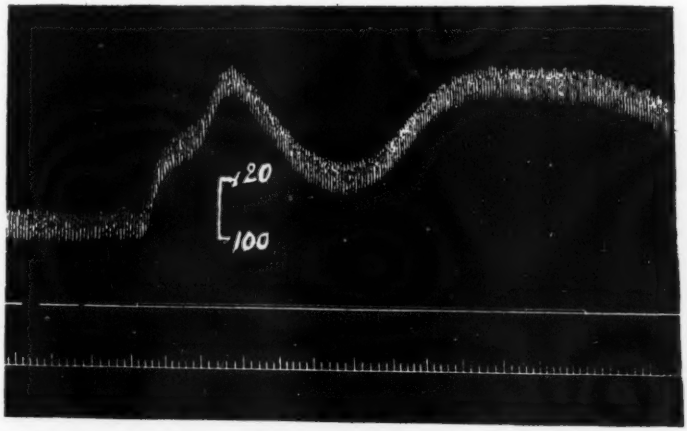

Fig 1. Dog, 12 K. Ether, vagi cut. Left Splanchnic stimulated in thorax. Time tracing in seconds.

At the outset it was found that the conditions under which the experiment is performed makes a very considerable differ-

ence in the character of the curve obtained by splanchnic stimulation. There may also be differences characteristic of the different species and of different conditions of the animal. V. Anrep seems never to have obtained in his dogs under normal conditions a form of curve which we now look upon as the typical or normal, namely, a sharp rise (having a "hump" about half-way up) followed by a marked "dip" nearly down to the original level, and succeeded by a rise which lasts as long as stimulation is continued. (See Fig. 1.)

This occurs in dogs under ether with both vagi cut. V. Anrep used A. C. E. mixture and morphia. Chloroform, curare, and morphia sometimes modify the curve in such a way as to abolish the "dip," leaving only the "hump" on the rise (See Fig. 2.)

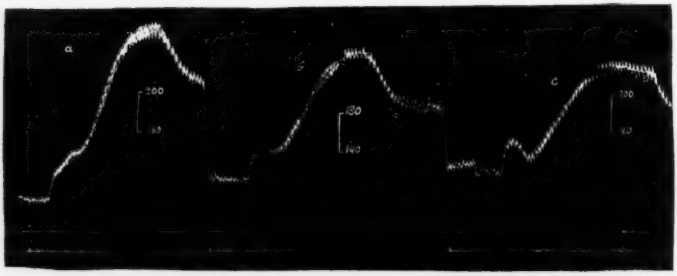

Fig. 2. Dog, 10 K. Ether, vagi cut, both splanchnics cut in thorax. a. Stimulation of left splanchnic five minutes after injection of 2 cc. of 1% morphine sulphate. b. Stimulation 15 minutes later. c. Stimulation 15 minutes still later. The effect of the morphine wears off and the normal curve tends to appear again.

In many of our tracings the "hump" and the subsequent "dip" are quite distinct (see Figs. 1, 2, 3) and the augmentation of the heart is very manifest (1, 2, 4, and others).

The curve just described is, we believe, to be regarded as the normal effect of stimulation of the peripheral end of the splanchnic nerve in the dog, as well as in the cat and the rabbit, when these animals are under the influence of ether alone, or under morphine and curare in addition, although under the influence of the latter drugs the "dip" is much less pronounced and sometimes altogether abolished.

V. Anrep, in discussing Elliott's results, says "Elliott investigated the question in the cat, in which animal the 'step' becomes a distinct fall." As we have already stated, in our experiments there was no essential difference in this respect between dogs and cats. The "step" referred to by V. Anrep is therefore not what we have called the "hump," but something which occurs later and which we call the "dip." We have not been able to convince ourselves that the nature of the normal curve is dependent on nervous or emotional conditions either in dogs or in cats.

According to Elliott the "dip" of the splanchnic curve in cats does not occur if the adrenal bodies are excised or tied off. V. Anrep reports that the "step" in dogs is in a similar manner abolished by suppression of the adrenal bodies. Gley and Quinquaud, on the contrary, believe that there is an important difference in the results between dogs and cats. They state that interference with the adrenal bodies does not affect the result in cats, and that it does so in dogs only because of a different anatomical arrangement. In their opinion, extirpation or ligature of the glands in dogs necessitates damage to nerve fibres, while in cats it may not.

According to our experiments there is no such difference in the results obtained in dogs and cats, respectively. Our results, indeed, entirely confirm those of Elliott and apply equally to dogs, cats and rabbits. We have usually obtained quite satisfactory positive results by simply clamping and unclamping the adrenal veins. Moreover, all necessary dissection in the neighborhood of the gland was carried out before the control experiment was performed. (See Figs. 3, 4.)

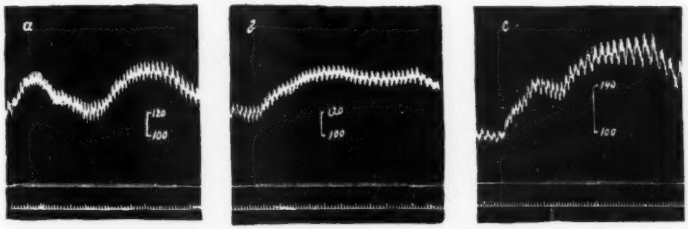

Fig. 3, Dog, 10 K. Ether, vagi cut, both splanchnics cut in thorax. a. Stimulation of left splanchnic. b. Do. after clamping adrenal veins. c. Do. after clamps have been released.

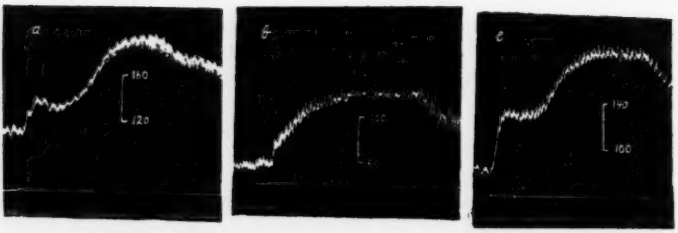

Fig. 4. Bitch, 10 K. Ether, morphia, vagi cut, both splanchnics cut in thorax. a. Left splanchnic stimulated. b. Left splanchnic stimulated after left adrenal has been tied off. c. Right splanchnic stimulated with right gland intact.

Fig. 5 shows that the results in the cat were similar to those obtained with the dog.

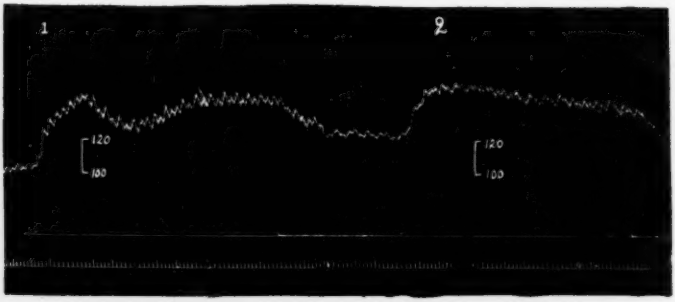

Fig. 5. Cat, 2 K. Ether, vagi cut, both splanchnics cut in thorax. 1. Right splanchnic stimulated. 2. Right splanchnic stimulated after the adrenal veins had been clamped on the right side.

During the period of the first rise of blood-pressure under splanchnic stimulation there is marked passive dilation of the denervated limb. This is followed by pronounced constriction. In experiments on this subject we have always employed ether, morphia, and curare. When the adrenal veins are clamped or tied this constriction does not occur. Thus, our results are in accord with those of V. Anrep. (See Figs. 6 and 7.)

V. Anrep believes that the constriction of a denervated limb during the pressor response to stimulation of the central end of the sciatic nerve is due to the action of adrenin. He

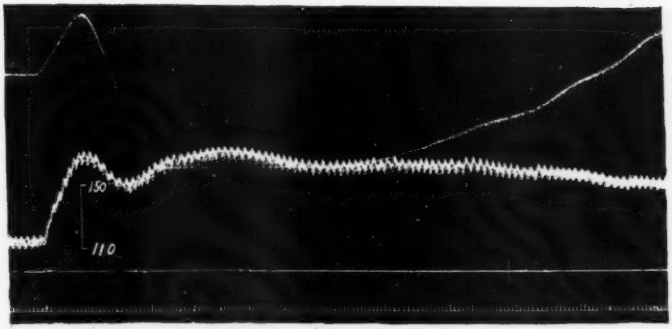

Fig. 6. Dog, 16 K. Ether, morphia, curare, vagi cut. Upper curve, volume of denervated hind limb; lower curve, carotid blood-pressure. Time tracing in seconds. The right splanchnic was cut in the thorax and the peripheral end stimulated.

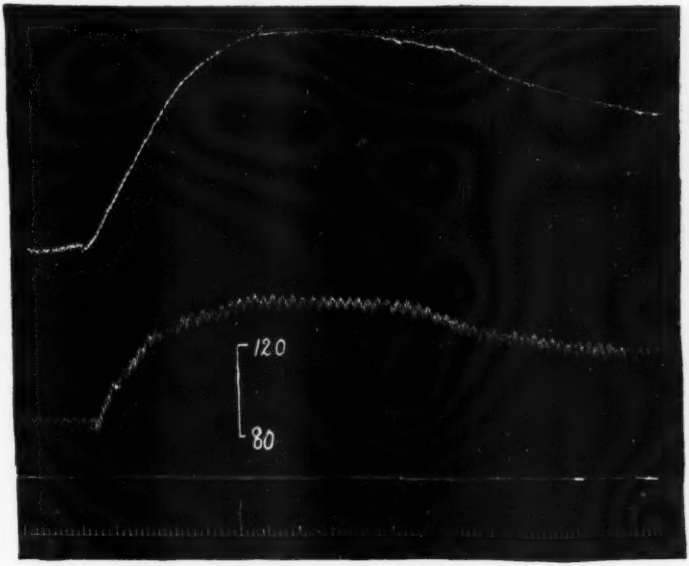

Fig. 7. Same dog as in Fig. 6. In this tracing we see the effect of stimulating the right splanchnic after the adrenal veins had been clamped on both sides.

was led to this conclusion by the observation that after removal of the adrenal bodies from the circulation, the limb does not constrict, but follows passively the blood-pressure. Our own results enable us to confirm this observation. (See Figs. 8 and 9.)

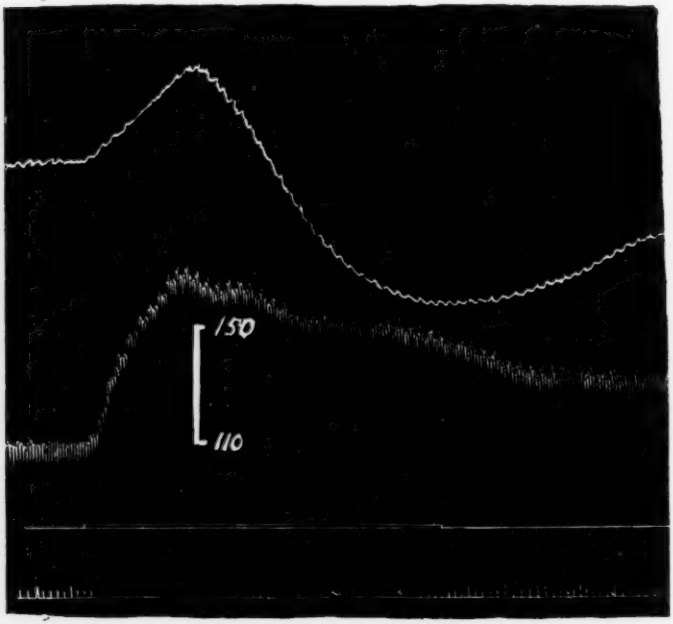

Fig. 8. Dog, 10 K. Ether, morphia, curare, vagi cut. Upper curve, volume of denervated left hind limb. Lower curve, carotid blood-pressure. The abdominal cavity was open and the adrenal bodies had been cleaned in readiness for tying off.

Although suppression of adrenal function does not appear to affect the alteration in blood-pressure brought about by vasomotor reflexes, yet it seems exceedingly probable from the above experimental results that, even when the limb is intact, the adrenals must play a considerable part in determining the distribution of blood in the body, when a stimulus is applied to an afferent nerve. It can scarcely be imagined that the presence of a nerve-supply can totally mask the action of the chemical

agent. But it is difficult to be certain that the adrenal bodies play a part in vaso-motor reactions in the normal state of the animal.

What follows after adrenal suppression when a weak stimulation causes a depressor response we have not ascertained.

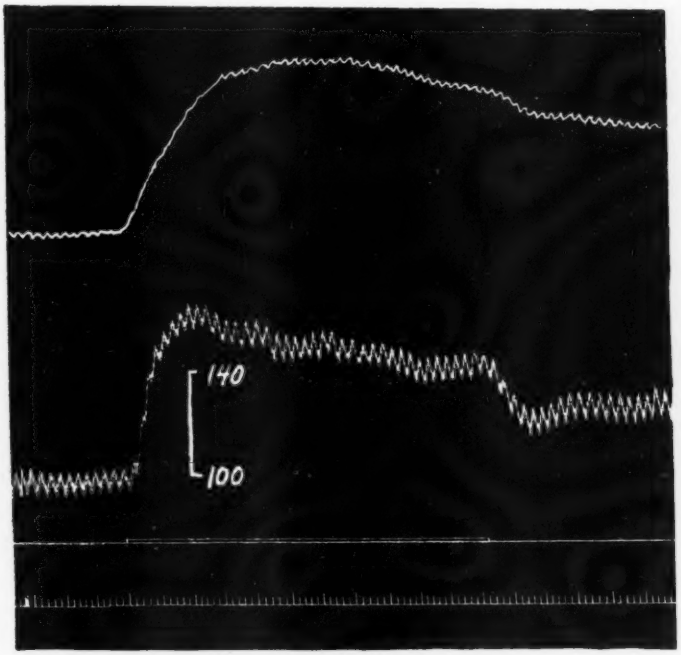

Fig 9. Same dog as in Fig. 8. The tracing is taken five minutes later than in Fig. 8, after the adrenals on both sides had been tied off. Stimulation of central end of right sciatic.

If we investigate the difference between the intact and the denervated limb in regard to their respective responses to injection of small doses of adrenin (0·2 c.c. to 1 c.c. of a 1:100,000 solution) we must bear in mind the results obtained by Hoskins, Gunning and Berry (12). It was found that with nerves intact adrenin causes active dilatation of the muscles

and vaso-constriction in the cutaneous vessels, so that while the entire limb usually constricts, a skinned limb will invariably dilate. This result we have been able to confirm. As further pointed out by Gruber (11), the results just described are obtained only when the nerves to the limb are intact. In the denervated limb, at any rate within a certain period after the denervation, adrenin does not cause active vaso-dilatation in the muscles. These results agree well with what we find, namely, that when the splanchnic nerve is stimulated peripherally and the sciatic centrally in such a way as to give pressor responses, the intact limb follows passively the blood-pressure, while the denervated limb constricts. It is only reasonable to suppose that this is a natural consequence of the fact that in the denervated limb the muscles do not actively dilate, and therefore fail to produce the masking effect upon the skin constriction. We have been able to satisfy ourselves on these points by injection of adrenin as well as by stimulation of the nerves just referred to. This is, in our opinion, to be regarded as a provisional answer to the query above, as to why the presence of intact nerves should interfere with the response to the chemical agent.

In regard to the effects of asphyxia, our results differ from those of V. Anrep. We have been unable to obtain tracings showing any significant difference in the behavior of a denervated limb during asphyxia in an animal with adrenals suppressed as compared with one in a normal animal.

It seems impossible to avoid the conclusion that when powerful impulses are transmitted along certain afferent or efferent paths, the adrenal bodies (or, more correctly, the masses of chromaphil tissue contained within these bodies) play a part in the total response. Whether, under normal condition of the animal, the impulses which are so transmitted are sufficiently powerful to give rise to results similar to those of the laboratory experiments, or whether they are of such a character as to be adequate for such results, we cannot pretend to say. It is tempting to assume that the impulses may become adequate in

physiological emergencies, as was suggested by Cannon and de la Paz (4).

It appears from our own tracings and from those of Elliott that, although the character of the splanchnic curve is seriously modified by elimination of the adrenals, the total rise of blood-pressure may not be affected, or may even be greater than before. It follows that in these cases the effect of the adrenin actually poured out into the circulation is a fall of blood-pressure and not a rise. This corresponds with the fact that small doses of adrenin produce a fall and not a rise. In other cases, however, the total rise is greater in the intact animal.

The question arises as to the nature of the process by which the adrenin is poured out into the circulation in sufficient quantity to produce, in laboratory experiments, the effects detailed above. It is generally assumed that the process is a true secretion, and that the splanchnic nerve is the channel along which the secretory fibres run. This is supposed to apply equally to experiments in which the splanchnic itself is stimulated and in those in which changes in the circulation are brought about reflexly by stimulation of different afferent nerves.

Some observers have alleged that the discharge of adrenin is the result of vaso-dilation of the adrenal body as a result of direct or reflex stimulation of its vaso-motor nerves. It would appear very extraordinary if stimulation of the splanchnic caused vaso-dilation in the adrenal bodies, while it caused vaso-constriction in all the other abdominal viscera to which it sends fibres. Moreover, the experimental evidence on this point is not satisfactory. We might even go as far as to assume for the present that stimulation of the splanchnic constricts the vessels of the adrenal body. If this is the case, the constriction of the vessels of the gland might actually be the cause of the discharge of adrenin. For a certain amount of this substance contained in the veins and capillaries of the organ would be almost instantly driven out into the general circulation. This effect

could of course be only of the briefest duration, though it might easily be sufficiently prolonged to produce the temporary effects above referred to. These effects as we have seen, consist practically in a fall of the carotid blood-pressure and a constriction of vessels in certain somatic areas. This theory would account for the fact, observed by Elliott, that it is not possible to completely exhaust the gland by continued splanchnic stimulation. It would also explain the fact that the effects above detailed cannot be repeated until a certain time has elapsed since the first stimulation. If this were found to be the true explanation of what happens, we should then not have to deal with a true secretory activity of the glands, but only a mechanical expulsion of adrenin as a result of vaso-constriction.

In all such discussions it is important to bear in mind that the medulla of the adrenal body constitutes only a portion of the total chromaphil tissue in the body. In fact, it seems more than likely that there is more chromaphil tissue outside the adrenal bodies than within them. We can scarcely avoid this conclusion when we remember that the tissue in question is distributed widely in the sympathetic ganglia and in masses of various sizes throughout the abdomen. (See Vincent, 17).

This being so, it is remarkable that elimination of the adrenal medulla alone produces such marked and definite results as we have described. In the case of the effects of stimulation of the splanchnic nerve, it may be that the stimulation produces greater or more direct effects on the adrenal medulla than on such structures as the "abdominal chromaphil body" (17), though the innervation of the latter would also be from the splanchnic. There is another possibility. Assuming that the glandular theory of adrenal activity is the true one, it might be urged that the adrenal medulla is a chromaphil gland of a more highly-developed type than that of the scattered masses of chromaphil cells in other regions.

Cramer (5) has recently come to the conclusion that an increased activity of the thyroid gland leads to an increased liberation of adrenin from the adrenal bodies. He has formu-

lated the conception that the thyroid and adrenal bodies form part of a mechanism for the chemical heat regulation of the body. He uses osmic acid vapor as a fixing agent to show the adrenin granules under varying conditions. The method has been applied to the adrenal bodies of mice and rats subjected to the conditions which were expected to produce alteration in the functional activity of the glands; these were thyroid feeding, thyroidectomy, injection of B-tetrahydronaphthylamine and other procedures. In all cases, he says, the method gave evidence of distinct changes in the medullary cells. There was evidence of the passage of adrenin granules into the blood-vessels of the medulla after injection of B-tetrahydronaphthylamine. The granules disappear if the glands are exhausted, and, in the various conditions demanding increased activity of the glands, fine black granules, similar to the granules of the medulla, appear in the cortex, especially in the layers of cells nearest the medulla. Cramer points out that this is clear evidence that the cortex takes part in the functional activity of the medulla and that these two parts of the gland are not two physiologically independent organs.

These observations, if confirmed, have a very important bearing on the question of the relationship between cortex and medulla of the adrenal bodies. Up to the present time there has been no satisfactory evidence that the two portions of the gland have any relation to each other, either embryological or physiological.

Even if it could be shown conclusively that under certain conditions adrenin granules are found in the part of the cortex next to the medulla, this would by no means prove that the cortex normally takes a part in the production of adrenin. It might be supposed that under pathological conditions adrenin might not be able to escape by the usual channels, and so would overflow into the neighboring cortex.

The histological evidence as to a secretory function of the adrenal medulla seems to us to be far from satisfactory.

SUMMARY

1. The typical blood-pressure curve obtained in response to stimulation of the peripheral end of the cut splanchnic nerve has the following characters:

There is first a sharp rise (having a "hump" about half-way up). This is followed by a marked "dip" nearly down to the original level and succeeded by a second rise. The pressure remains high as long as stimulation is continued.

This curve is obtained in dogs, cats, and rabbits, and although it is perhaps most typical of what occurs in animals under simple ether anesthesia, yet with slight variations it may be expected to represent the usual sequence of events under morphine and also under curare.

2. When the adrenal veins of both sides are clamped or tied, or when both splanchnic nerves are cut and the adrenals clamped or tied off on the side stimulated, stimulation of the splanchnic nerve gives rise to a simple curve without the "dip."

This is true in dogs, cats, and rabbits, and is not determined by any damage done to nerves in manipulation of the glands, but to an interference with the pouring out of adrenin into the blood-stream.

3. The "dip" in the normal curve is due to the discharge of adrenin in such doses as to produce a depressor effect.

4. When splanchnic (peripheral) and sciatic (central) nerves are stimulated in such a way as to give a pressor response, the intact limb follows passively the blood-pressure, while the denervated limb becomes constricted. This is due to the fact that in the recently denervated limb the blood-vessels of the muscles do not actively dilate (as they normally do) and therefore fail to mask the skin constriction.

5. After elimination of the adrenal bodies the denervated limb also follows passively the blood-pressure. There is now no constriction on stimulation of the above nerves.

6. It would appear that the general result of a discharge of adrenin into the circulation, over and above the amount which normally passes out into the blood, would be a constriction in the skin area and a vaso-dilatation of skeletal and cardiac muscles. It is obvious that this might be of advantage in certain physiological emergencies.

7. It seems probable that the chromaphil tissue, especially, perhaps, the so-called "medulla of the adrenal" may have

important functions connected with the distribution of blood in the body, if not under normal conditions, at any rate, in times of nervous and muscular strains.

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DEATH PRODUCED BY TYING THE ADRENAL VEINS

F. A. Hartman and W. E. Blatz

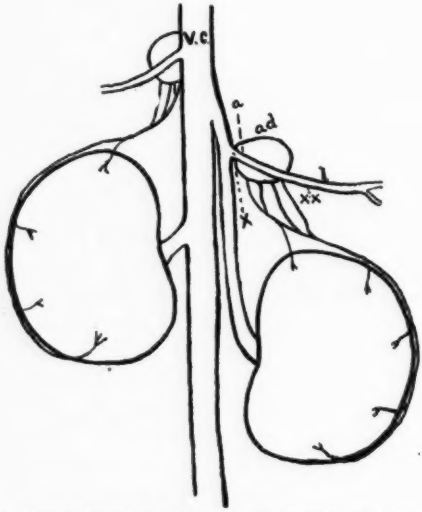
(From the Department of Physiology of the University of Toronto)

Since the discovery that Addison's Disease is due to disturbance of the adrenal apparatus, many attempts have been made to produce the disease artificially. Adrenal insufficiency is said to be the main cause, and hence epinephrectomy was thought to be the best method of producing the peculiar syndrome of the disease. This method is, however, too drastic, the animal succumbing more or less rapidly to the operation. Some method of reducing the adrenal function without completely destroying it, appeared to be required.

Certain infectious diseases impair the function of the adrenals. Diphtheria (1) produces vacuolization and hemorrhage in the adrenals, and diphtheria toxin (2) is said to lessen the pupil-dilating substance in the adrenal venous blood. In view of this we attempted to destroy a portion of each gland by the injection of sublethal doses of diphtheria toxin into the exposed gland. Evidently the toxin was either neutralized, or else washed away by the blood stream before it could cause much destruction of the adrenal tissue, because no symptoms could be noticed, following such injection. Although we experimented with only one cat and one guinea pig, the method was considered unsatisfactory.

The blood flow through the adrenals is relatively very large; therefore by hindering the blood supply we should be able to produce degenerative changes rather easily. If the blood flow could be almost stopped, the changes in the gland might be slow enough to produce merely a condition of hyposecretion, such as we desired. The arteries break up into such fine branches before entering the capsule, that checking the inflow would be too difficult. On the other hand, the outflow is mainly through a large vein emptying into either the vena cava, or else the renal vein, so that by ligation the flow could easily be stopped. However, a small amount of blood escapes

through a rete of vessels connecting the adrenal with the kidney (3) so that occlusion of the adrenal vein does not produce complete stasis of blood in the gland. (See accompanying figure.)



Veins to the adrenal of the cat. The rete of vessels connecting the adrenal with the kidney, after the diagram of Cow.
ad., adrenal.
a., common lumbo-adrenal vein.
l., lumbar vein joining the adrenal vein.
v. c., vena cava.
x., position of ligature.
xx., ligature here in some experiments, in addition to position x.

This research is a preliminary study of the effects produced by disturbing the blood supply to the adrenals.

Methods

A lumbar vein from the dorsal musculature joins the adrenal vein as the latter leaves the gland (Fig.) so that their blood is carried by a common trunk into the vena cava. In some cases one adrenal was excised. In all of the experiments the common lumbo-adrenal vein was completely tied off (see X in Fig.) central to the adrenal or adrenals left in the body.

Because of the possibility of a back flow through the lumbar vein, this was also tied in a few animals (XX, Fig.). All

animals were anesthetized with ether and the operations conducted aseptically. Cats were used in a majority of cases, but dogs and rabbits occasionally.

After the operation the animals were studied at first daily, and then at longer intervals to see whether characteristic symptoms developed. They were examined for changes in rectal temperature, weight, heart rate and muscular weakness. In some cases the animal was killed, in others it was allowed to die following the natural course of events. The adrenals were then fixed and studied.

The glands were placed for twenty-four hours in a mixture of 90 parts of 3.5 per cent $K_2Cr_2O_7$ with 10 parts of 40 per cent formaldehyde (4). They were then washed in running water for an equal time, after which they were immersed in a solution of Gum Arabic for a few hours before sectioning.

Sections 5 micra to 30 micra in thickness were cut with a freezing microtome. After washing in tap water to remove the gum, the sections were stained 5 to 10 minutes with Delafield's haemotoxylin, subsequent treatment with water removing the excess stain. They were finally left in a saturated 70 per cent alcoholic solution of Sudan III over night. After again washing with water they were mounted for study in Farrant's medium. The lipoids were stained red by Sudan III and chromaffin cells yellowish if they contained adrenalin.

Results

Experiment 1. The adrenal veins to both glands in a cat were tied off by ligating the vein coming from the lumbar muscles and the common vein as it entered the vena cava. The only possible outlet from the adrenals was the kidney rete. Forty-eight days later the animal died without developing any noticeable symptoms except muscular weakness just before death. Microscopic examination of the glands showed a slight vacuolization in the zona fasciculata and the presence of adrenalin in the medulla. Lipoids were plentiful in the cortex.

Experiment 2. The right adrenal was excised and both the lumbar vein and the common lumbo-adrenal vein tied off on the other side. The cat died two days later with no observed external change. The adrenal which had remained in the animal was much congested with blood. The superficial veins of

the kidney on the same side were also congested. The two glands were compared microscopically. The appearance of the left adrenal was very striking. Adrenalin instead of being limited to the medulla was disseminated throughout the gland, being especially concentrated in the cells of the zona glomerulosa. Adrenalin in the zona fasciculata and zona reticularis was found between the cell columns, but was absent from the cells. The total quantity of adrenalin was much greater in the left adrenal than in the right, as indicated by the staining. There was considerable vacuolization in the zona fasciculata.

Experiment 3. The lumbar and lumbo-adrenal veins were tied on the left side, the right adrenal being left intact. The animal in this case was a dog. Eighteen days later the animal was killed, and the two adrenals fixed. No great difference was observed between the two glands. There was less lipoid in the ligated gland, there being great numbers of large lipoid bodies in the cortex of the normal gland, while these were largely absent from the ligated gland.

Experiment 4. The lumbo-adrenal vein where it entered the vena cava was tied off on both sides, but the veins to the lumbar muscles were not touched. This animal, a rabbit, gained in weight during the next thirty-two days. It died seventy-five days after the operation. Upon microscopic examination the presence of adrenalin was not found. Lipoids were very scant in amount.

Experiment 5. After removal of the right adrenal the lumbo-adrenal vein from the left gland was tied off, the vein from the lumbar muscles being left intact. The animal (cat) was operated upon at 4 p. m.

At nine o'clock the next morning the pupils were still greatly dilated, and constricted much less than did those of a normal cat when exposed to a bright light. The most striking thing, however, was the marked pilomotor effect. The hair was erect all along the dorsal surface, and to a certain extent, on the tail. The heart was beating at the rate of 140 per minute, whereas before the operation the rate was 250. The rectal temperature was 35.7° C.

Forty-one hours after the operation, the pupils had become nearly normal, while the pilomotor effect still persisted, but

was not quite so marked. The heart rate was 184 beats per minute. The rectal temperature was 37.2° C.

In four days the cat appeared normal except for a slight pilomotor effect. Later certain changes were apparent. The hair on the face was falling out. The hair on the ears had become quite scanty. There was a red coloration on the inner side of both forelegs. The cat began to cry incessantly and lost weight. Eruptions appeared on the skin of the face (46 days after the operation).

Sixty-eight days after the operation, the weight had been reduced from 2.500 kgm. to 2.060 kgm., in spite of its eating well. The rectal temperature was 39.1° C. The hair was very scraggy and unkempt. The cat was irritable, but weaker than normal. It was not so active, largely on account of muscular weakness, because it still appeared restless. The heart rate was normal (249). At this time there was considerable difficulty in micturating. It took several minutes to expel the urine.

Ninety-five days after the operation, the heart was still normal in rate, the temperature still high (39.0° C.) and the weight partly regained (2.350 kgm.). It appeared a little stronger, but still walked with a stiff-legged gait. The fur was still in a poor condition, the longer hairs, such as the vibrissae, being broken and scraggy.

The cat died 128 days after the operation. It had been gradually losing weight so that it was reduced to two-thirds the original, viz., to 1.750 kgm. The day before death it appeared very much as it had for weeks. (Death was hastened the last two or three days by a marked fall in the room temperature.)

Upon post mortem everything was found well healed. The lumbar vein to the left adrenal was much enlarged. The adrenal weighed 0.426 gm. Lipoids were fairly plentiful in the gland, but did not seem to be entirely confined to the cortex. Some adrenalin was present, as shown by the yellow stain.

The kidney on the same side had been fixed and stained in the same manner as the adrenal. Many of the blood vessels in the outer zone were stained yellow. Scattered here and there tubules and glomeruli were found similarly stained. It appeared that adrenalin brought to the kidney directly from

the adrenal was being excreted in the kidney. However, this observation needs further confirmation.

Experiment 6. A second cat was operated upon in the same way as in the preceding experiment. Within two hours after the operation the pupil had become normal. Eight hours later there was a decided pilomotor reaction along the back. In 13 hours the pilomotor effect had become slight. No other changes appeared. The animal died 18 days later. It had been eating well up to that time.

There were only slight traces of lipoid in the cortex of the adrenal which had been left in the animal. There were also traces of lipoid in the medulla. Adrenalin if present at all was extremely scant.

Experiment 7. The adrenals of a third cat were treated as in the two foregoing cases. Three hours after, there was a marked pilomotor effect, but no dilatation of the pupil.

The pilomotor effect persisted for 38 days. At that time the animal appeared weaker. The temperature and heart rate remained about normal. The animal died 59 days after the operation. It had fallen off slightly in weight, from 1.34 kgm. to 1.22 kgm.

Histologically, the adrenal which had remained in the animal was almost devoid of lipoids, the small amount present being in the cortex. No trace of adrenalin was found.

Experiment 8. A dog was operated upon as in the preceding experiments. It recovered without showing any decided symptoms. The rectal temperature 10 days after the operation was 39.2° C. The animal was killed 83 days after the operation. Its weight had fallen from 5.1 kgm. to 4.6 kgm. Histologically, the adrenal gland which had remained in the animal differed very little from normal.

Experiment 9. In order to determine how much pressure might be produced in the lumbar vein when the lumbo-adrenal vein was tied, we fastened a cannula into the former vein immediately after the latter had been tied. A large dog (18 kgm.) was used while under ether anesthesia. The cannula was connected with a long vertical glass tube containing a little half-saturated Na_2SO_4 solution.

The pressure in the tube gradually rose as follows:

Time in minutes	Increase mm. ½ sat. Na_2SO_4 Sol.	Total pressure mm. ½ sat. Na_2SO_4 Sol.
1	155	155
2	109	264
3	93	357
4	81	438
5	71	509
6	60	569
7	47	616
8	38	654
9	30	684
10	26	710
11	19	729
12	19	748
13	12	760
14	9	769
15	6	775

The final pressure attained in the glass tube was 775 mm. or 73.25 mm. in terms of Hg. Arterial pressure at the same time was 77 mm. of Hg.

Discussion

The method which we have used does not produce death nearly so quickly as does the removal of both adrenals. In that case death occurs in a few hours to a few days (5). Six of the seven animals, in which the veins from the adrenals had been tied, died in 2, 18, 48, 59, 75 and 128 days respectively. Experiment No. 3 should not be included because one gland was left intact in the animal. Experiment No. 8, on a dog, was the exception, the animal being killed after 83 days. At the time of death, however, it was losing weight.

Three of the animals which died of their own accord, showed symptoms of weakness some time before death; in the other three, no changes were observed. In regard to the histological changes, three of the animals showed no presence of adrenalin, and only a trace of lipoid in the adrenal after death, while three others showed both adrenalin and lipoid in larger amount. Of course, the absence of adrenalin in a gland which

is not fixed immediately at death indicates little, for adrenalin disappears very soon. But in any case, judging from the lipoids, with the exception of experiment No. 5, the adrenal function was much below normal.

Cat No. 5 was very exceptional and may have been a case of hyperactivity of the adrenal. Many of the symptoms tend to indicate that. It is quite possible that in this instance the increased pressure produced by tying the common lumbo-adrenal vein stimulated the cells of the adrenal to greater activity. The increased pressure may also have produced a back-flow of blood through the lumbar vein and thus through anastomoses into the general circulation. In fact, this was possible in all the animals where the lumbar vein was not tied, because the pressure attained is nearly as great as arterial pressure (experiment No. 9).

Summary

1. After having the veins to the adrenal glands tied an animal lives much longer than after double epinephrectomy, but eventually dies.

2. There is evidence that the adrenals function for a considerable time after such an operation, the secretion escaping through the rete of vessels leading to the kidney, and possibly by back flow through the lumbar vein, when that is left open.

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THE SIGNIFICANCE OF EPINEPHRIN IN MUSCULAR ACTIVITY

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Since 1855 (1), a symptom-complex has been linked with the destruction of the suprarenal glands or the chromaffin system in general. This disease, "*Morbus Addisonii,*" is characterized by muscular and vascular asthenia, irritation of the stomach, pigmentation of the skin and changes in the blood picture.

Abelous, Langlois and Charrin (2) showed that persons suffering from this malady were less capable of doing muscular work, than were individuals suffering from pulmonary tuberculosis. According to Langlois this myasthenia can be markedly diminished by organotherapic measures. After six weeks treatment with suprarenal extract, the subject of their investigations was able to lift a weight 5.8 times longer and the highest contractions were four times as high as those recorded before the treatment.

Such a marked improvement is not always observed. In fact the results obtained by the different men and by the same men working on different patients vary a great deal. Adams (3) has collected from the literature reports of ninety-seven cases with the following results: seven were made decidedly worse, forty-three derived no benefit, thirty-one showed marked improvement and sixteen cases showed permanent relief after organotherapic treatment.

Daland (4) reports good results with the use of therapeutic doses of epinephrin in a case of Addison's disease.

There is a great deal of difference of opinion as to the seat of the lesions. Marakascheff (5), after studying the adrenal glands in cases of Addison's disease and in certain conditions in which the glands were the seat of marked pathological change, concludes that the cortical substance is particu-

larly involved and destruction of this portion of the gland may be followed by the entire symptom-complex. He claims that the medullary substance may be completely destroyed without the presence of the malady. If one adrenal is destroyed, hypertrophy of the cortex of the other may take place; this hypertrophy leads to great compression of the medulla. His views are supported by Lowy (6), who claims that complete absence of the specific cellular elements of the cortex of both adrenal glands will produce typical symptoms of Addison's disease. The adrenal glands he examined were composed of medullary parenchyma only.

Wiesel (7) on the other hand cites six cases in which the chromaffin cells in the medulla of the adrenals and in the sympathetic system were destroyed. The cortex of the adrenals and of the accessory adrenals was found intact or only slightly affected and he believes Addison's disease to be a specific disease of the chromaffin system.

Be that as it may, it is safe to suppose that the function of the cortex of the gland may be different from that of the medulla. Such a possibility is suggested by Hoskins and Wheelon (8). It may be that in those cases in which the cortex as well as the medulla is diseased epinephrin has little or no action, whereas in those cases in which only the medulla is affected the epinephrin is of the highest service to the patient in relieving the symptoms caused by its deficiency in the circulation.

Marked betterment in the height of muscular contraction has been reported by Trerotoli (9), who studied the effect of adrenalin in human beings, upon muscles which had been fatigued either by voluntary or by electrical excitation. He observed that 1 mg. of adrenalin injected subcutaneously prolonged the record of contraction.

According to Cannon (10) epinephrin plays a definite rôle in enabling the individual to meet successfully the emergencies of life. Various major emotions, pain, fear, and rage cause a reflex secretion of epinephrin, which assists in the execution of the physical counterparts of the emotions; combat, flight *et cetera*. The muscles, which are chiefly concerned in these, are benefited to the greatest extent by the epinephrin discharge.

The inhibition of intestinal peristalsis, the constriction of the splanchnic and cutaneous vessels and the dilation of the vessels in the muscles themselves (11) cause a shifting of the blood from the bowel and skin to the muscles to meet the extra strain about to be put upon them. The hyperglycaemia produced furnishes the muscles with an additional food supply and the dilation of the bronchioles (12) assists in supplying more oxygen for the crisis. Furthermore, efficiency of a fatigued muscle is greatly improved by epinephrin, by the means already mentioned, and probably also by some action on the fatigue products (13), and within certain limits the coagulation time of the blood is diminished to meet the emergency of hemorrhage (14). All these conditions function for the superiority of the individual and for the preservation of his life.

That epinephrin is invaluable in rapid recovery from fatigue is borne out on experimental animals. Albanese (15), Boinet (16), Abelous and Langlois (17), Abelous (18), and Hultgren and Andresson (19) and Biedl (20) found that animals in which the suprarenals were removed died shortly after the operation. They also found that the life of the animal could be prolonged slightly by the injection of suprarenal extract. Myasthenia occurred in all cases and Abelous and Langlois and Albanese concluded that the function of the adrenalin was to neutralize or destroy the toxins set free in muscular work. These experiments upon experimental animals support the view that muscular vigor and power is dependent upon the epinephrin set free by the suprarenal glands. It must be remembered, however, that the life of these epinephrectomized animals could not be prolonged more than twenty-four hours by the injection of epinephrin. It seems, therefore, that something is lacking in the commercial epinephrin and as has been suggested, is possibly supplied by the cortex of the adrenal glands.

If epinephrin is essential for prolonged muscular efforts, it would be natural to suppose that some change should be noted in the cells proper of the suprarenal glands after such exertions. Changes have been observed. Battelli and Boatta (21) and Carl (22) found that the adrenals are exhausted of their

adrenalin, after prolonged muscular fatigue. Such a change was also noted by Ingier and Schmorl (23) in patients suffering from Addison's disease in which there was marked myasthenia. Not only is there a depletion in the glands of their epinephrin but they also undergo histological changes. Bernard and Bigart (24) and Bardier and Boone (26) observed the cells to contain numerous vacuoles after prolonged muscular activity. Since other glandular cells and also nerve cells develop vacuoles after activity the inference can safely be drawn that these suprarenals are active as well as are the muscles, during the period of exertion. Some interrelation must, therefore, exist between muscular work and the chromaffin system.

The results of the experiments which have been performed to determine the effect of epinephrin upon non-fatigued and excised, fatigued muscles are not uniform. Oliver and Schäfer (26) and Boruttau (27) claim that adrenal extract increases the height and prolongs the periods of contraction in non-fatigued muscle. These results are contradicted by Kuno (28) Takayasu (29) and by Schäfer in his later work (30). Takayasu found adrenalin to have a depressing action similar to that observed by Boruttau (26) in some of his experiments.

Dessy and Grandis (31) report that adrenalin produces a beneficial effect on fatigued salamander muscles, either when injected subcutaneously or when added to the solution in which an isolated muscle is contracting. Cannon and Nice (32), Hoskins (p. 185) and also the author (unpublished experiments) after repeated attempts have been unable to confirm Dessy and Grandis' observations in frog's muscles similarly exposed to the adrenal extract. The author also demonstrated that the threshold stimulus of a non-fatigued muscle was not affected by adrenalin (33). Panella (34), Radwánska (35), Cannon and Nice (37), and Gruber (36) showed conclusively that adrenalin betters the height of muscular contraction in a muscle undergoing fatigue. Cannon and Nice demonstrated that adrenalin injected in small doses or secreted by the glands during splanchnic stimulation, improved the activity of the fatigued muscles, in some cases by more than 75 per cent. These results were corroborated and extended by me in a series of researches,

the results of which were published a few years ago. I showed that adrenalin increased the height of muscular contraction when injected intravenously in small doses (0.2 to 0.5 mil. of a 1:100,000 solution) and that the same dose administered in the same manner would bring back in five minutes or less the increased threshold stimulus caused by fatigue of the nerve-muscle or muscle as would rest of one to three hours (36).

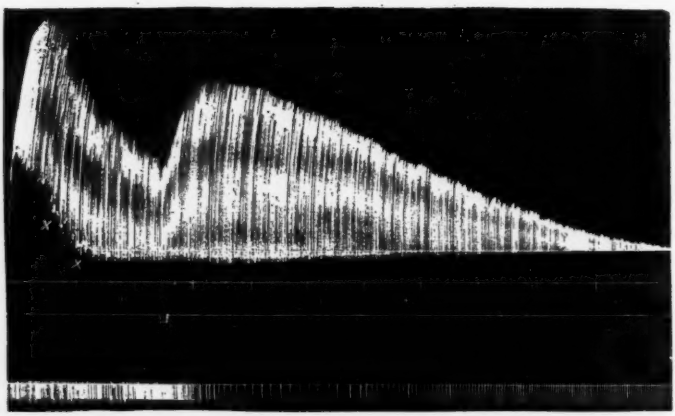
The question as to how adrenalin produces this beneficial action is still unsettled. Hoskins, Gunning and Berry (11) attempted to explain this as due to a bettered circulation. Epinephrin, however, can produce vaso-dilation in the muscle vessels only when the nerves are intact, or, after nerve section, only when some time (4 to 10 days) has elapsed (36). I have never been able to get vaso-dilation of muscle vessels immediately after cutting the nerves leading to the muscles. Moreover in muscle electrically excitated (2 to 4 times per second) there are three factors tending to bring about extreme dilation of the vessels: first, the nerves are severed, and the vasomotor tonicity from the vaso-motor center, therefore, inoperative (37); second, the rate of stimulation is favorable to dilation (38); and third, as Kaufmann (39) has shown, active muscles presupposes actively dilated vessels. Under these conditions one would scarcely expect adrenalin to produce further dilation. Yet under these circumstances epinephrin does exert a beneficial influence.

Experiments were performed in which the epinephrin was injected into the perfusion fluid of a fatiguing muscle. (See accompanying figure.) It was noted that invariably vasoconstriction resulted with a betterment in the height of muscular contraction. This betterment was dependent upon the strength of the adrenalin injected. In one case a 27-fold betterment was obtained by injecting 0.5 mil. of 1:1,000 solution of epinephrin (36). This substance is therefore not a depressant, as stated by Takayasu.

From the experiments upon animals, the inference can be drawn that epinephrin betters the height of muscular contraction in two ways; first by its specific effect upon the muscle in eliminating fatigue and in addition, in those animals in which the nerves are intact by bettering the circulation through the

muscle by its vasodilator qualities. Whether or not the specific action is due to neutralization, or destruction of the fatigue products, the rapid formation of more available energy or due to some toxic action thus increasing the excitability of the muscle cannot be definitely stated.

Some investigators attempted to throw light upon this subject by noting the antagonistic action of the so-called fatigue



Upper record, muscular contraction of the anterior tibial muscle of a cat, contracting 120 times per minute pulling against a spring with an initial tension of 75 gms. Below it the time in half minute intervals. The lowest record is the rate of flow of the perfusion fluid from the venous cannula. (× — ×) Adjusted muscle lever so that the muscle was after loaded. At the point indicated on the lower middle line 1 mil. of a 1:100,000 solution of epinephrin was injected into the perfusion fluid. There resulted an increase in the height of contraction of 92 per cent, but a decrease in the rate of the perfusion fluid of 91 per cent.

products and epinephrin. Carnot and Josserand (41) studied the vasoconstrictor qualities of epinephrin before and after fatigue. They found that 0.05 mg. of epinephrin per kilo body weight injected into the femoral artery, with the leg at rest, produced a rise in blood pressure of 10 cm. of mercury. After tetanizing the opposite leg for fifteen minutes, 0.055 mg. of epinephrin per kilo body weight was injected into its femoral artery and the systemic blood pressure rose only 1.5 cm. of mercury. They claim, rightly, I believe, that the epinephrin

was destroyed or neutralized by the fatigue products.

That the reaction of a muscle after fatigue is acid to litmus has been known for more than half a century. Ranke (41) in 1865 proved definitely that paralactic acid, monopotassium phosphate and carbon dioxide are some of the products given off during the process of fatigue. Lee (42), Burridge (43), and Schenck (44) were able to reproduce the fatigue curve by irrigating muscles with the above products. Ryffel (45) reported an increase in lactic acid in the urine after severe muscular exercise. Gruber and Kretschmer (46) and Gruber (47) were able to corroborate Lee's and Burridge's results and they demonstrated that epinephrin possesses the ability to restore almost to normal the height of contraction of muscles artificially fatigued by the injection of lactic acid, sarcolactic acid, monopotassium phosphate and monosodium phosphate.

An acid reaction is also developed in muscles approaching a state of *rigor mortis*. Here as in fatigue the reaction is the result of the accumulation of lactic acid. Fletcher and Hopkins and Fletcher noted that most of the lactic acid in frog and mammalian muscles was produced before *rigor mortis* had been reached. The muscles were still flaccid and irritable. Just as in artificially fatigued muscles, so also here, epinephrin showed a marked ability to restore irritability and contractility to the nerve-muscle. In some of the experiments performed by Gruber and Fellows (48) epinephrin caused a 29-fold increase in the height of the contraction, in others the irritability, which was lost, as shown by electrical excitation of the nerve, was restored by the perfusion of the drug through the muscle. In many instances the animals had been dead for from 1 to 3 hours.

Here again epinephrin must have acted either antagonistically to the substances formed during the death of the animal, or it increased the production of available energy for the contraction of the muscles or it affected the tissues directly, producing an increased excitability and contractility.

It was noted by Cannon and Gruber (49) that dilute solutions of epinephrin increased the rate of the oscillatory variations observed in rhythmically stimulated muscles, providing the quantity was sufficient to cause a betterment in the height of muscular contraction. A strong dose of adrenalin sufficient to

produce a marked constriction of the arterioles (1 mil. 1:10,000 injected intravenously) resulted in a lessened height of muscular contraction and a slowing of the waves. If this decreased blood supply persisted for a long time a temporary disappearance of the waves resulted.

In many of the experiments performed upon perfused, excised muscles the betterments were so marked and the vasoconstriction so striking that only one conclusion can be drawn, *i. e.*, epinephrin exerts some specific action upon fatigued muscle other than that due to mere circulatory changes.

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ACTION OF SOME OVARIAN AND CORPUS LUTEUM EXTRACTS ON THE PUPIL OF THE FROG'S EYE

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The authors have been engaged for some time in studying the pharmacological and physiological properties of various glandular extracts. In connection with these studies, systematic observations have been made concerning the effect of such extracts on the pupil of the frog's eye, inasmuch as it is well known that certain hormones such as epinephrin exert a marked influence on that organ. It is deemed desirable to report in the present communication the findings concerning the action of some ovarian and corpus luteum extracts on the frog's pupil.

The preparations used in this research were the desiccated lutein of the sow prepared by the Hynson, Westcott, and Dunning Company without admixture of any preservatives, and the desiccated ovarian substance of the sow, marketed by Armour and Company. Further experiments were also made with fresh corpus luteum substance of the sow and with the fresh ovary of the same animal. The extracts employed were prepared by treating the glands with cold physiological saline or with Locke's solution. In most cases, whether the fresh gland or the desiccated product was employed the concentration of the extract was made to be equivalent to 10 per cent of the fresh gland. This 10 per cent extract when desired could be diluted by adding saline. Occasionally a 20 per cent extract was made.

The results obtained on the pupil of the frog's eye are interesting and are expressed in the subjoined table. It was found that the corpus luteum extracts whether prepared from the fresh gland or from the desiccated product, produced a distinct dilatation of the pupil in from 30 to 60 minutes, depending upon the concentration employed. Ovarian extracts, on the other hand, were found to produce very little or no change in

the size of the pupil. Inasmuch as the ovarian preparations which were used contained small quantities of corpus luteum, the slight dilatation noted after the use of such extracts may be ascribed to the lutein content. The difference between the effects of the ovarian and corpus luteum extracts, however, is so great that we are forced to regard the ovary and corpus luteum in so far as the effect on the pupil is concerned as being very different glandular bodies. This of course agrees well with all other data so far known concerning the independent and distinct function of corpus luteum.

TABLE

CORPUS LUTEUM				TIME	CONTROL			
Strength	Drug	Diameters of Pupil Before	After		Strength	Drug	Diameters of Pupil Before	After
		m.m.	m.m.	min.			m.m.	m.m.
20%	Desiccated	2.7x1.5	3.4x2.2	30	20%	Ovary	2.7x1.7	3.0x1.9
"	"	2.3x1.6	3.0x2.4	15	"	"	2.5x2.0	2.9x2.6
"	"	2.6x1.9	3.0x2.3	140	"	"	2.8x2.3	2.7x1.8
10%	"	2.8x1.6	3.5x2.3	25	10%	"	2.8x1.8	3.1x2.0
"	"	2.3x1.8	3.3x2.9	45	"	"	2.6x2.0	3.0x2.8
"	"	2.3x1.7	3.0x2.6	10	"	"	2.6x2.1	2.8x2.2
"	"	1.8x0.9	2.5x1.5	60	Locke's Solution		1.7x0.8	1.7x0.9
"	"	2.1x1.5	2.5x2.0	60	Locke's Solution		2.5x1.7	2.0x1.7
"	"	1.9x1.5	2.5x1.7	40	10%	Ovary	2.1x1.5	2.3x1.5
"	"	2.3x1.7	3.0x2.5	30	"	"	2.5x1.8	3.0x2.2
"	"	2.8x2.5	3.0x2.5	60	"	"	2.8x2.4	3.0x2.6
"	"	2.3x1.7	2.6x1.9	30	Locke's Solution		2.1x1.5	2.2x1.6
"	"	2.5x2.0	3.0x2.6	20	10%	Ovary	2.5x1.9	2.6x2.0
"	"	2.5x2.0	3.0x2.5	10	"	"	2.5x2.0	2.5x2.0
"	"	2.9x2.3	3.0x2.6	20	"	"	2.9x2.3	3.0x2.4
5%	"	2.9x2.1	3.0x2.3	40	5%	"	2.9x2.0	2.9x2.0
"	"	2.5x1.8	2.6x2.0	60	"	"	2.6x1.9	2.8x2.1
"	"	2.5x1.8	3.0x2.0	30	"	"	3.0x1.5	3.0x1.8
"	"	2.8x1.6	3.0x2.3	20	"	"	2.7x1.6	2.5x1.3
"	"	2.5x1.5	2.7x1.8	80	"	"	2.7x1.7	2.7x1.8
"	"	2.1x1.3	2.8x2.0	45	"	"	2.3x1.3	2.5x1.6
20%	Fresh	2.1x1.6	2.8x2.5	25	20%	"	2.1x1.8	2.7x1.9
10%	"	2.3x1.8	2.7x2.1	20	Locke's Solution		2.2x1.5	2.3x1.7
"	"	2.3x1.7	2.6x1.9	..	Locke's Solution		2.1x1.5	2.2x1.6
"	"	2.6x1.7	3.0x2.5	20	10%	Ovary	2.6x1.7	2.7x1.8
"	"	2.7x2.0	3.2x2.6	25	"	"	2.7x2.0	2.8x2.0

THE PHYSIOLOGIC ACTION OF THYROXIN

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In 1914 (2) the physiologic action of the iodin compound occurring in the thyroid was in part described. At this time it was stated that after the administration of this substance to dogs there was in every case a long delay before any physiologic effects were demonstrable. The action was described as follows:

"When injected subcutaneously in animals, there is at first no effect on either the pulse-rate or the blood-pressure. After from twenty-four to thirty-six hours the dog appears restless, has a slight increase in temperature, and a decided increase in pulse-rate. If a series of injections is given on successive days, these symptoms are aggravated, and after two or three injections they are accompanied by a distinct tremor, loss of weight, and severe diarrhea. On the fourth or fifth day of injection the pulse-rate is between 200 and 300, and all the other symptoms continue with increased severity."

While the problem concerning the physiologic action of thyroxin is not yet completed, certain progress has been made which will be reported at this time. The iodin compound which in 1914 was tentatively named the "alpha iodin" compound in order to differentiate it from the other iodin compounds occurring in the gland which were called "beta," has now been given the name "thyroxin."

Further investigation has confirmed the delay in the action of thyroxin in animals and also in man, both in the normal condition and in myxedema. In a long series of patients suffering from myxedema who have been treated by intravenous injection of known amounts of thyroxin, Plummer has found that in all except two there was a very marked delay in the action of thyroxin. In these two patients there was a short-lived immediate response, but the prolonged action of thyroxin was noted as usual and the curve of the response after the first few hours was approximately the same as that given by the other patients.

Some of the early observations on the delayed action of thyroxin were obtained on goats. A series of eleven goats was injected daily with 14 mg. of thyroxin. The first goat died after eleven days and the rest followed at short intervals, all dying within thirty days. This shows that the long-continued presence of thyroxin in the animal organism is incompatible with life and it also suggests that death is not caused from the toxic action of the substance itself, but from secondary reactions. In order to bring this out more clearly another normal goat was injected with 230 mg. of thyroxin in a single injection. This amount was one and one-half times as much as was required to kill the first goat of the series, and yet the single injection of this relatively enormous dose produced almost no demonstrable effect, and the goat, even from the second day after the injection was, to all intents, normal.

Massive doses of thyroxin have also been given to dogs. Some were injected with thyroxin while they were receiving intravenous injections of sugar or of amino acids. In a few of these animals it was possible to demonstrate an immediate response to thyroxin, but this response very rapidly subsided and a long delay period followed before there were definite signs of the functioning of thyroxin.

Since the successive daily administration of thyroxin brings about death, and a single injection of enormous doses produces, in most instances, no demonstrable effect, we may conclude that the thyroxin molecule per se is not toxic to the animal organism. Although the intravenous injection of thyroxin produces no change in blood-pressure, pulse-rate, nervous manifestations, or any of the so-called hyperthyroid symptoms, the long-continued presence of thyroxin within the tissues of the body produces the picture of hyperthyroidism in its entirety, terminating in great emaciation and eventually in death. One factor, therefore, which would determine the reactivity of thyroxin would be the speed with which the tissues absorb thyroxin from the blood-stream. Even though thyroxin is circulated through the tissues of the body in the blood-stream, if the tissues refuse to absorb it from the blood it obviously could not produce its normal physiologic action. In order to determine whether or not the tissues do remove thyroxin from the

blood, 200 mg. were injected at once into the saphenous vein of a dog, and the bile and urine were saved for the next fifty hours. The bile and urine were analyzed for iodin and it was found that 43 per cent of the total iodin contained in the thyroxin injected was excreted in the bile within fifty hours, and 13 per cent was excreted in the urine during the same time. This accounts for a large amount injected and, while the thyroid gland of this animal was not analyzed for iodin, it is highly probable that the remaining amount injected was removed from the blood-stream by the thyroid gland and there retained, making practically 100 per cent of the injected thyroxin unavailable for functioning within the tissues.

Marine (3) and others have shown that the thyroid absorbs iodin when present in the blood and there can be little doubt that the gland absorbs and holds thyroxin, so that between the liver, the kidneys, and the thyroid gland, the excess of thyroxin is adequately cared for, and the tissues from a single injection do not take up enough thyroxin to result in a demonstrable physiologic response.

While no demonstrable physiologic response follows a single injection of thyroxin, there is no doubt that there is a physiologic response even to very small amounts. By the determination of the basal metabolic rate it may be shown that the myxedematous patient responds to exceedingly small amounts of thyroxin given in single injections. By "demonstrable response" is meant the increase in pulse rate and nervous manifestations with loss of weight, such as are observed when several administrations of thyroxin are given. The difference in the condition in the dog after one injection of thyroxin and after five injections is very striking, even though the weight of thyroxin given in the single injection is as great as the total amount used in the five injections.

Since the absence of thyroxin from the organism results in a lowered level of metabolic rate and the administration of thyroxin determines the basal metabolic rate in the myxedematous patient, it seems highly probable that under normal conditions an equilibrium exists between the thyroxin in the thyroid gland, the amount in the blood-stream, and the amount in the tissues. It is probable that the amount in the tissues fluc-

tuates according to the energy demands of the body, but that there is always an equilibrium seems highly probable. Under these conditions, if a large amount of thyroxin is injected into the blood-stream and nothing is done calling for an increased thyroxin content of the tissues, the tissues apparently are unable to absorb more thyroxin than their normal content and the excess is treated as a foreign substance and is promptly excreted in the bile. Some portion, however, is either excreted unchanged in the urine or is broken down and thus excreted. If thyroxin is injected on several successive days the amount in the thyroid gland, the amount in the liver, and the amount in the blood, eventually pass the normal limits for an appreciable period of time, with the result that the tissues are forced to absorb more than their normal content of thyroxin. When this process has started and secondary effects are brought into play the tissues are stimulated to such a height of activity that they, themselves, demand more thyroxin, and so the physiologic response is slowly built up. The full effect of the stepping-up process, however, is a matter of days, not a few hours. The tissues, once they have absorbed the thyroxin and begin to function at a higher rate of activity, in turn may affect the other ductless glands, especially the adrenal, as suggested by Cannon (1), and the increased activity of the adrenal, in turn, produces its train of effects.

Quantitative studies of thyroxin by Plummer (4) have shown that not only is the appearance of physiologic effects of thyroxin delayed in man, but the duration of the effects is surprisingly long, and the maximum effect from a single injection of thyroxin in myxedematous patients is not reached until the tenth day. After reaching the maximum effect, thyroxin still continues to function for another eight to ten days, so that the length of time a single administration of thyroxin functions within the body is about three weeks.

What chemical reactions are so stimulated by thyroxin that life is incompatible are still unknown; but it is obvious that death is not due, in a strict sense, to the presence of thyroxin itself, but is due to the secondary effects which thyroxin brings into play.

One of the most important findings in connection with the

physiologic activity of thyroxin has been the establishing of the quantitative relation between thyroxin and the basal metabolic rate. Plummer has shown that 1 mg. of thyroxin in an adult weighing approximately 150 pounds increases the metabolic rate 2 per cent. The curve of this response has been shown to be approximately a straight line between metabolic rates 30 per cent below normal to 15 to 20 per cent above normal. This finding, coupled with the observation that all myxedematous patients tend to approach a uniform metabolic rate which is about 40 per cent below normal, is extremely strong evidence in favor of the hypothesis that without the presence of thyroxin within the animal organism, rapid and large fluctuations in energy output would be impossible. Clinically this is substantiated by the great difficulty the myxedematous patient manifests when endeavoring to walk upstairs or carry out any other muscular activity. Their range of fluctuation of energy output is limited. Their normal existence is at a rate in the neighborhood of 40 per cent below normal. However, by the administration of thyroxin this basal metabolic rate can be raised to any desired figure, and it can be so maintained over periods of time measured in years. These facts suggest that in the normal animal organism thyroxin is not fundamentally essential to life. The fundamental chemical reactions occur and life is maintained in the complete absence of thyroxin, but in this condition the flexibility of energy output is limited to a narrow range. The addition of the thyroid apparatus to the animal organism establishes not only a higher plane of basal energy output, but it supplies the mechanism which permits the maximum range in flexibility of energy output. The amount of thyroxin within the tissues is undoubtedly a physiologic constant, a figure as constant per weight of tissue as the normal number of red cells per cubic millimeter of blood, etc. What determines this normal content of thyroxin is unknown. What maintains the content of thyroxin within the tissues is obviously the blood-stream. Some work has already been completed in this laboratory which has the objective of determining the thyroxin content of the blood and tissues. This may be done by determining the maximum iodin content of the blood and tissues. Whether or not the total iodin in the blood and

tissues is 100 per cent in the form of thyroxin or 50 per cent cannot be shown, but the total amount of thyroxin could not be more than the amount indicated by the total iodin present in the tissues. The method for the determination of iodin which was published by the writer in 1914 has recently been further refined and perfected so that now one part of iodin in ten to twenty millions can be determined with a high degree of accuracy. By the use of this method it has been shown that the iodin content of the blood of animals is approximately 1.5 to 2 parts per ten millions; that is, 15 to 20 one-thousandths of 1 mg. per 100 c.c. The iodin content of the tissues is slightly higher, averaging 2.5 to 3 parts per ten millions; and the content of the liver is still a little higher, from 3.5 to 4 parts per ten millions. These figures must be amplified and confirmed by still more work, which is now being carried out, but they already indicate that there is an equilibrium existing between the amount of thyroxin in the blood, in the tissues, and in the liver.

If the presence of thyroxin within the tissues determines the metabolic activity of the tissues it is obvious that if there were no mechanism for varying the amount of thyroxin and if the tissues always contained enough thyroxin to permit of their maximum output of energy, the control of the energy output during periods of rest would be, to say the least, difficult. Whether or not the thyroxin content of the tissues diminishes after a period of great exertion, the thyroxin being carried back to the thyroid gland by means of the blood-stream and there held as a reservoir until further demanded, is still unknown.

This mechanism is at least indicated and is in part substantiated by the findings of the seasonal variation of the iodin in the thyroid gland. Seidell and Fenger (5) have shown that during the winter months the thyroid glands of beef, sheep, and hogs all contain much less iodin than during the summer months. It is apparent that during the winter months more energy is required to maintain body temperature, and the low iodin content of the gland could be explained either by the fact that the thyroid gland has given up its supply of thyroxin to the tissues or by an actual wearing out of thyroxin

due to the prolonged functioning of the substance in the tissues, so that during January, February, and March the amount left in the gland would be at a minimum. During the summer months with less energy production in the animal, the amount of thyroxin demanded in the tissues is less. It reappears in the gland, either because its rate of production is greater than its rate of destruction, or because the amount in the tissues is returned to the gland and held there for use at some future time. The seasonal fluctuation of thyroxin in the gland is more satisfactorily explained on this basis than on the basis of varying iodin content of the food, and as it holds for beef, sheep and hogs, it is suggestive that the mechanism of the variation is essentially due to the varied energy output of the animals during the cold and the hot months of the year.

In conclusion, the physiologic action of thyroxin is probably that of a catalyst which bears a quantitative relation to the production of energy within the tissues, and the curve representing this relation is a straight line; that is, the increase in energy production with an increasing amount of thyroxin is simply an additive one. The substance appears to function within the tissues, and there is an equilibrium between the amount in the tissues, the amount in the blood-stream, and its source of supply, the thyroid gland. The entire absence of the substance from the body does not produce death, but merely a lowering of the level at which energy can be produced by the animal organism. In administering more than the normal amount of thyroxin to the animal organism there is a distinct lag in the absorption of the compound by the tissues and there is a rapid return to the normal content if the administration of the substance is stopped. The chemical reactions which are brought into play by the administration of thyroxin are probably not different from the fundamental chemical reactions occurring in its absence. As a catalyst it merely increases the rate at which these fundamental reactions are carried out. The thyroid apparatus apparently has been added to the animal organism in order to permit a greater range of flexibility of energy output than would exist without such a mechanism.

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CLINICAL STUDY

A NEW POINT OF VIEW IN APPROACHING THE DIAGNOSIS AND TREATMENT OF A PATIENT

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Physicians have been so intensely occupied with the study of disease by methods of precision which have been developed to extend the range of their five senses, that they have forgotten to a large extent the subject of disease—Man. Physical diagnosis itself, with its capacity for illuminating the abnormal condition, was an added technique of the same nature as the present more elaborate method of examination provided by adaptations from laboratories of pure science. Obviously, as new methods made disease processes more approachable to investigation, the interest and attention of observers was drawn even more keenly to the pathological phenomena. The natural outcome of this interest has been to establish the present habit of medical thought which focuses primarily upon the pathological process.

The teaching in all medical schools is designed to develop among medical students the capacity to detect various disease entities. The system of physical examination which has become so firmly rooted, has enabled physicians to detect consolidations of the lung, cardiac murmurs, enlargement of liver and spleen and the presence of masses where masses do not belong. The typical history and description of the phenomena of all the known disease entities have been carefully compiled and the student is practiced in comparing his "case" with the accepted descriptions of the diseases. If one observes the history and the physical examinations on the charts of any good hospital it becomes at once evident that the primary object of the record is to establish the presence of a definite disease and give it a name. The whole plan upon which the history is taken and the physical examination executed is designed to demonstrate some pathological lesion. If this lesion is discovered, the object of the search has been accomplished. But

except for the description of the specific lesion of each case, if it should be found, the remainder of the physical examination and history would fit equally well any other patient in the ward.

In the matter of history taking the stereotyped form of inquiry as to the health of the parents is definitely directed toward answering the question, "Is this disease before us one which has been acquired from parents?" In the same way the record of the patient's past disease experience is designed to narrow the diagnosis to those maladies for which he has not developed an immunity by reason of a previous attack. The physical examination then proceeds to search for the lesions; and when the lesion is found, the most careful and minute description of it entered upon. Histories and physical examinations of this character when carefully carried out are productive of as much knowledge as the purely clinical side of medicine of the moment can be, and from this point the laboratory has been called upon to amplify our understanding. But here, again, we meet the same point of view, and the laboratory is utilized as were the history and the physical examinations to demonstrate the pathological process.

The question with which this discussion attempts to deal is, whether there may not be some other method of approach to the study of disease more illuminating than the present one. Contemplation of the great epidemic diseases has indicated definitely that there is such a thing as racial susceptibility to infection. The appearance of diabetes and arterio-sclerosis in the Hebrew race points to a tendency of physiological nature. One also hears, not infrequently, of family susceptibility; in the latter instance the word susceptibility is perhaps not so well chosen as would be the word tendency or characteristic. But at all events, in these two expressions of racial and family differentiation may be found the germ of an approach to the problem of disease which is not carried into the study of the affliction of the individual. In other words, with the individual, cognizance has not been taken of the kind of human material in anticipation of the kind of disease. Obviously, the first step in shifting our point of view from the study of the disease process primarily, to a study of the subject, is to de-

velop a method of history and physical examination which will make each individual stand out from the rest of humanity as sharply as the black race does from the white. We must subject the individual who comes for advice and relief from suffering to an analysis that is directed in the first instance toward an understanding of his personality, and by the term personality in this sense is not meant his psyche alone. The study of personality should include an analysis of his anatomical individuality, as well as his physiological, psychological and immunological characteristics. This method of approach, by these four definite avenues, must not be limited alone to physical examination, but must pervade the taking of the history and the use of whatever specialized and technical forms of examination are at our disposal. And the findings along each of these avenues of study must be correlated and considered with the greatest care.

With our increasing knowledge of the still shaded territory of the endocrine glands it is becoming evident that there is some connection between body conformation, body function, psychic activity and possibly also between immunity forces and these glands. That anatomical features are definitely associated with the action and interaction of the endocrine system is now generally accepted in the condition of acromegaly, myxedema, Graves' disease and Addison's disease. The diagnosis of these maladies up to the present time has depended to a large extent upon the changes in the surface and bony anatomy of the individual. It may further be assumed that the disturbances of various body functions found in this group, are analogous phenomena in the domain of physiology.

Indeed, in this group there has been made a fairly complete correlation between the anatomical and physiological and psychological changes. Thus, in Addison's disease we associate pigmentation and unusual distribution of hair with the asthenia as forming two important elements in the picture. The usual method of history and physical examination, however, does not include as routine a particular study of the points upon which the diagnosis of this group of maladies is based. And yet, these disturbances produce in a striking measure what is meant in this paper by personality. The acromegalic

giant; the nervous, irritable, ineffectual individual with hyperthyroidism; and the subdued, gloomy, tired patient with Addison's disease, are well known characters in hospital wards. Is it possible that by taking these types as yard sticks by which to measure individuals whose personalities are less striking to the casual observer, we may gradually come to an understanding of the more subtle differences between individuals, and so to a better knowledge of their success or failure in the face of attack by disease or under the stress of life?

In the plan for the study of patients which follows, it will be found that there is little, as a matter of fact, which has not been included in other schemes of physical examinations, but the arrangement of the material is such that it helps primarily to study the personality of the patient. In the course of this examination any pathological deflection which would have been detected by the routine method will not escape. But instead of occupying the center of the stage and focusing the interest of the study upon itself, the lesion will automatically assume a perfectly logical position in the general plan upon which the individual is designed by nature.

PERSONALITY STUDY

I. ANATOMICAL:

HISTORY: Family: shapes and sizes.
Patient: a. Size at birth.
b. Growth and development (before puberty).
c. Age of appearance of secondary sex characters.
d. Growth and development after puberty.
e. Dentition history.

PHYSICAL EXAMINATION: A. Outward, anatomical markings as per Chart I.

CHART I

WEIGHT: HEIGHT:
GENERAL CONFORMATION:
HEAD: Shape: Length: Width:
Shape of face: Profile:
Eyes: Deep set: Interval: Squint:
Exophthalmic: Motions:
Oedema: Palpebral fissure: (width:
(direction:

Glabella:
Supraorbital Ridges:
Nose: Size: Form:
Ears: Size: Shape:
Lobe:
Jaws: Tongue:
Teeth: Spacing Color: Quality:
Position: Shape: Repair:
NECK: Length: Girth:
HANDS: Shape:
Fingers: Nails:
SHOULDERS: Breadth: Form:
CHEST: Girth: Sub-costal angle: Waist: Girth:
PELVIS: Width at crests Trochanters:
TRUNK: Length: Upper Extremities: Length:
Lower Extremities: Length:
HAIR: Scalp:
Eyebrows: Space: Color:
Thickness: Supratemporal recessions:
Arch:
Outer end: Cyclic growth changes:
Beard: Chest:
Abdomen: Axilla:
Back: Suprapubic:
Thighs: Arms:
Legs: Forearms:
GONADAL SYSTEM: Varicocele: Prostate:
SKIN: Texture:
Pigmentation:

B. Inward Markings as per Chart II

CHART II

ROUTINE EXAMINATION OF:

a. Eyes: pupils, and fundi and visual fields:
b. Heart and circulation by usual methods:
   1. percussion.
   2. auscultation.
   3. X-ray.
c. Routine examination of lungs; lymphatic system.
d. Routine examination of abdomen, liver, spleen.
e. Routine examination of prostate and female internal genitals when indicated.
f. Reflexes:
g. Blood count and differential.
h. X-ray of sella turcica, epiphyses, etc.

II. PHYSIOLOGICAL:

HISTORY: Family: a. Food idiosyncrasies.
b. Bowel habit.
c. Sweat habit.
d. Mother's menstrual and pregnancy.

Patient: a. Food idiosyncrasies.
b. Digestion.
c. Bowels—constipation.
d. Urine, quantity, frequency, influence of emotion.
e. Reaction to external temperatures.
f. Sweat: amount.
localization.
g. Heart: sensations.
rate on exercise and emotion.
h. Respiratory mechanism:
sensation of choking.
inability to get breath, etc.
i. Physical strength and fatigue.
j. Sex functions:
Females: Menstruation:
age at onset,
pain,
duration,
interval.
Pregnancies:
toxemias,
labor.
Breasts and lactations.
Males: Maturation age,
Libido,
Potentia.

FUNCTIONAL EXAMINATION: (see Chart III)

CHART III

a. Gastric juice.
b. Stool examination.
c. Kidney function test—Urine examination.
d. Heart and circulation:
1. Blood pressure,
2. Influence of exercise,
3. Arrhythmias,
4. E. K. G.
5. Polygraph.
e. Peripheral circulation—Capillary Pulse.
f. Flushing.

g. Tache.
h. Respiratory mechanism:
   1. Arrhythmias,
   2. Voice and speech (stammering),
   3. Gas exchange (basal metabolism).
i. Response to glandular extracts:
   1. Adrenalin (Goetsch test),
   2. Thyroid,
   3. Pituitary,
   4. Ovarian,
   5. Drugs—pilocarpin.
j. Sugar tolerance.
k. Skin irritability: Hives.

III. PSYCHOLOGICAL:

HISTORY: Family: general nervous pattern.
Patient:
a. Development in childhood—advanced, backward.
   1. Impatient to get on, etc.
   2. Frights in childhood.
   3. Early permanent ideas.
   4. Difficult or tractable child.
   5. Dreams.
b. Adult life.
   1. Characteristic or average psychic state.
      sluggish, recessive,
      alert, projective.
   Accomplishments.
   Fears.
   Ambitions.
   Repressions.
   Interests.
   Talents.
   Sleep: Dreams.

EXAMINATION: 1. Binet test,
2. Psycho-analysis,
3. Dream analysis.

IV. IMMUNOLOGICAL:

HISTORY: Race:
Family: Tendencies to infectious disease.
Patient:
a. Infectious disease history
   Especial attention to relationship of age to disease.

b. Tendency to sore throat, quinsy.
c. Tendency to small boils.
d. Tooth root and gum infections.

EXAMINATION:

a. Serological reactions:
   1. Widal,
   2. Wasserman—Blood and spinal fluid,
   3. Gold reaction—Spinal fluid,
   4. Agglutinations.
b. Bacteriological:
   1. Cultures,
   2. Smears,
   3. Dark field examinations,
   4. Pneumococcus grouping,
   5. Animal inoculation.
c. Immunity test:
   1. Schick reaction,
   2. Tuberculin test, etc.

It will be seen from a study of these charts that the patient is investigated as completely as the means now at our command permit in each one of the four domains which together determine the personality of an individual. It is necessary to investigate each domain separately with regard to history and methods of examination and then with the four sets of studies, side by side, one can correlate the findings in each. It is interesting to note when a considerable series of individuals has been studied in this way, that through each, one finds the expression of the same forces which seem to determine the extreme forms mentioned above as representing known disturbances of the endocrine system. Thus, for example, it is striking to find that the individual who wakes very early in the morning, who has a greatly increased tremor after drinking coffee, who has hair line on the forehead that grows very high, with recessions over the temples, whose skin is delicate and pink and white, also disclaims having had any infectious disease with the possible exception of typhoid, malaria or tuberculosis. When the total metabolism of this individual is studied it is found to be above the normal. Or, one finds, for example, an individual of extremely dark complexion, with unusually deep pigmentation, normally disposed, an excessive growth of hair and low growing scalp line, or with freckles on the eyelids, who is able to work for half a day with

considerable success, but who then becomes so fatigued that the latter part of the day finds him good for nothing. The immunological history and examination of this individual may indicate that he has had diphtheria, or that he is the subject of a positive Schick reaction. Physiologically this patient may suffer from hyperacidity. Again, an individual may be met who discloses to anatomical study a large, flabby frame, prominent upper jaw with widely spaced teeth, no hair on the chest and a transverse suprapubic arrangement. Physiological study of this individual will reveal that he has an increased tolerance for sugars. The history of his anatomical deveolpment will indicate that he was a large infant and always continued above size. In his immunological history one may find reference to some sort of brain fever or possibly infantile paralysis or mumps.

And so by correlating the histories and the examinations in each of the four panels it is possible to come to a far clearer understanding of the forces which determine the form and function of mind and body, their strength and weakness and susceptibility to infection. The study of the individual dominates and surrounds the study of his affliction and it is amazing how frequently the particular pathological disturbance belongs irresistibly in the whole fabric of his personality.

"LA ACCION FISIOLOGICA DE LOS EXTRACTOS HIPOFISIARIOS." By Dr. Bernardo A. Houssay, Professor of Physiology in the University of Buenos Aires, 1918, pp. 281 and bibliography, pp. 75. A. Flaiban, Buenos Aires.

To sundry good reasons for a wider knowledge of the Spanish language another has been added by the appearance of this monograph by Prof. Houssay. It is the result of ten years of intensive study and embodies many hundreds of individual experiments.

Whether the term "physiological" is justified in this caption is discussed in a prefatory section. It is used, at any rate, in a somewhat loose sense since one section of the book is explicitly devoted to toxicology. That various of the pharmacodynamic effects described are actually physiological remains to the reviewer, at least, somewhat doubtful.

The first chapter is a profusely illustrated account of the comparative morphology of the hypophysis with a brief concluding section on its chemical composition in different animals. Its high content in cholestrol is emphasized. Next the literature on the pharmacodynamic effects of various extracts is exhaustively reviewed and the author's own contributions summarized, with several illustrative graphs. A brief abstract of this chapter has been published in Endocrinology, 1917, **1**, 393. A closing section reviews the methods of assaying pituitary extracts.

Chapter 3 takes up the technique of preparing extracts of various parts of the gland and the comparative pharmacology of these. It concludes with a discussion of the commercial preparations, the nomenclature and the preservation of extracts.

The next section exhaustively treats of the toxicology of hypophyseal extracts. This is followed by a ten-page discussion of the effects in different organs of the administration of pituitary materials.

Chapter 6, of 30 pages, is devoted to the effects of extracts prepared in various ways on the circulation in different organs. A shorter chapter takes up the effects on the heart. This is illustrated by mechanical and electro-cardiograms.

Succeeding chapters are devoted to the effects on the blood, on respiration and on various sorts of smooth muscle and on

skeletal muscle. On p. 164 is reproduced a graph showing a beneficial effect of posterior lobe extracts on an isolated fatigued gastronemius which is strikingly similar to those published by Gruber on the effects of adrenin in the intact animal. The next sections take up the effects on growth, development and metabolism.

Possibly the most noteworthy chapter in the book is the 14th, devoted to the influence of hypophyseal extracts on the various secretions, and particularly that of milk in the human and other species. This comprises 50 pages.

Five brief chapters devoted to effects on the nervous system, "the alleged antitoxic action of hypophyseal extracts," comparative physiology of the active principles of the hypophysis, comparative action of adrenin and hypophyseal extracts, and "the adrenal-hypophysis association," complete the discussion.

A review of a work of this sort is necessarily inadequate since the wealth of details can not be summarized. Some of these have been included in a series of abstracts in Endocrinology (1917, **1**, 359, 372, 393, 533; 1918, **2**, 64, 94, 162, 171, 187, 325, 478 and 497), but on many points the original must be consulted.

The book concludes with an exhaustive bibliography of 75 pages. The greater part of the references have been obtained at first hand. The source of those otherwise derived has been indicated. The utility of the bibliography is unfortunately curtailed, as the author admits, by the translation of all the titles into Spanish. Most of the titles quoted, however, are fairly comprehensible to one with but a modicum of knowledge of the specific language employed.

At any rate, so thoroughly has the work been done that no one for years to come can safely publish research on any phase of the subject treated without consulting this monograph.

—R. G. H.

ABSTRACTS

ACROMEGALY with intense diabetes and change of hair color (Akromegalie mit intensiven Diabetes und Wechsel der Haarfarbe). Ausch (D.) Med. Klinik (Berl.) 1918, **14,** 131-33.

A case is described in which ante-mortem X-ray examination showed an enlarged sella turcica. The diagnosis was confirmed post-mortem. The change of hair color from fair to dark has not previously been described in acromegaly. Physiol. Abst., **3,** 267.

ACROMEGALY without hypophyseal tumor and the pathogeny of same (Zur kenntnis der Akromegalie ohne Hypophysentumor und die pathogenese derselben). Yamada (S.) Mitt. a. d. med. Fac. d. k. Univ. z. Tokyo, 1918, **8,** 411-41.

The case is reported of a young merchant who had had excellent health until the age of 17, when he noticed that his hands and feet were growing larger. This fact he attributed to his sound health. He developed edema, hypoesthesia of the calves and finally lassitude and fatigue. Marked depression of sexual inclinations was noted. At the time of his death from beriberi at the age of 21 the enlargement of the limbs was very marked. At autopsy the hypophysis was found normal both in gross and microscopic appearance; there was no evidence of augmented secretion granules. The thyroid was hypertrophic and the thymus "persistent." The testes were atrophic and spermatogenesis depressed. The pineal contained masses of colloid. The adrenal medulla was hypertrophic. The case was therefore, seemingly, polyglandular in origin. The paper is illustrated with 5 rotogravure plates.—R. G. H.

ADIPOSIS DOLOROSA. Cecikas (J.) Grèce médicale (Athens) 1918, **20,** 1-5 (French supplement to Iatriki Proodos).

Cecikas reports a case in a man of 32, married for six months, which, he thinks, throws light on the etiology of the disease. The pressure of the man's body against his desk ex-

plained the unusual location of the lipomas, and the immediate effect of an injection of pituitary extract on retention of urine confirmed the influence of the pituitary on the innervation of the bladder, but the primal factor in Dercum's disease seems to be some abnormal or lacking hormone from the organs of reproduction. This seems to upset the normal balance in the chromaffine system. His patient was clinically cured, even to the retrogression of the lipomas, by systematic treatment with extract of thyroid 1 part, extract of pituitary, 1 part, and of ovary 2 parts, supplemented by a vegetable diet and exercise in the country. Whenever this treatment was interrupted, the whole set of symptoms returned, even including some of the tumors. The patient learned to make his organotherapeutic products himself, making a cold extract of thyroid and testicles, 1:4, from sheep 1 or 2 years old. (Extraction cold; 50 c.c.; phenol, 0.05.) He took a teaspoonful of this extract morning and evening in warm soup. Cecikas recalls that Dercum in describing his first case of adiposis dolorosa noted its connection with the thyroid.—J. Am. M. Assn.

ADRENAL insufficiency, Acute. Boyd (W.) J. Lab. and Clin. Med. (St. Louis), 1918, **4**, 133.

A soldier upon admittance to the hospital was sinking into coma. The limbs were rigid, reflexes gone, pupils dilated, face and hands cyanosed, temperature 99° F. The urine was normal, lumbar puncture negative, Wasserman reaction negative. Death occurred in less than six hours. The autopsy showed pulmonary tubercular lesions. The stomach contents showed no trace of poison. The adrenals were almost entirely destroyed, and converted into structureless, amorphous, yellow masses. They were firm in texture and were considerably larger than normal. No trace of adrenal tissue could be found on the right side; on the left side a small strip only was present. This consisted almost entirely of cortex. The remainder of the gland consisted of areas of necrosis surrounded by endothelial and giant cells, characteristic of tuberculosis. No trace of medullary substance remained. The case appears effectually to disprove the theory that the medulla of the adrenal is essential to life. The entire medulla must have been completely destroyed for a considerable time, and yet the patient possessed sufficient physical vigor to engage in the full duties of a military camp. The persistence of a small amount of cortical tissue on the left side strongly suggests that this is the part of the gland which is necessary for the maintenance of life and that the destruction of this tissue beyond a degree compatible

with life gave rise to symptoms of acute adrenal insufficiency. —H. W.

ADRENAL crises (Nebennierenapoplexie). Loewenthal. Berl. klin. Wchnschr, 1918, **55,** 1126.

In case of acute infections, and from other causes, "apoplexie" in both adrenals may occur. The symptoms are abdominal pain; intestinal spasms with constipation; perspiration; weak, irregular, slow pulse and normal temperature. The disease is always fatal. The symptoms may be explained as due to diminution in circulating adrenin.—J. K.

ADRENAL, Focal necrosis of the, with remarks upon acute adrenal insufficiency. Moschowitz (E.) Proc. N. Y. Path. Soc., 1917, **17,** 127-129.

Published elsewhere. See Endocrin. 1918, **2,** 472.

ADRENAL form of malaria. Fraga (C.) Rev. Ibero-Americana de Ciencias Medicas (Madrid) 1918, **40,** 9-20.

Fraga reports from Brazil three cases of a set of symptoms indicating acute insufficiency of the suprarenals, and explained by malarial infection. One of the patients was demonstrated at a meeting of the American Society of Tropical Medicine at New York. Necropsy in one case showed the malaria parasites in the capillaries of the suprarenal cortex. The importance of this suprarenal form of malaria is enhanced by the fact that we have in epinephrin a means to tide the patient past the danger point. In the algid form, artificial serum with epinephrin given by the vein, may complete the triumph of quinin. In the less severe cases opotherapy alone may prove effectual. J. Am. M. Assn., **71,** 1447.

ADRENAL gland, Functional activity of the medulla of the — of the tuberculous (De l'activité fonctionelle de la glande médullaire surrénale des tuberculeux). Porak (R.) Annales de Méd. (Paris) 1918, **5,** 404-416.

Extracts were made of the glands of patients dying of tuberculosis in various forms. The extracts in each case caused a marked increase in arterial pressure when injected intravenously in rabbits. The hypotension of tuberculosis is due, therefore, to some other cause than adrenal deficiency. A considerable amount of theorizing is included, in which no atten-

tion is paid to the various pertinent researches of recent years on adrenin pharmacology.—R. G. H.

ADRENAL glands with toxic infections. Manie (A.) Ann. inst. Pasteur, 1918, **32,** 97-110.

The subcutaneous administration of adrenin has no preventive action against tetanus intoxication. When the two are injected separately they remain ineffective against each other. Only their mixture exposed at 37° insures innocuousness of the toxin. Experimental evidence is given of the inactivity of adrenin administered under these conditions. Chem. Abst., **12,** 1361.

(ADRENAL) Contributo allo studio della malattia di Addison nell' infanzia (Addison's disease in a girl aged 10 years). Rutelli (G.) La Pediatria (Napoli), 1916, **24,** 274-81. Abstr. Brit. Jour. Child. Dis., 1919, **16,** 61.

There was a history of enlarged cervical glands at the age of 10 months, and an affection of one finger which resulted in ankylosis at the age of two years. Pigmentation of the skin commenced at the age of 4 years. The blood pressure was 65-70 mm., and there was marked asthenia. The urine was normal excepting for slight diminution in elimination of uric acid and creatinin. On a diet rich in carbohydrates, sugar appeared in the urine 20 hours after an injection of one mg. of adrenalin; on ordinary diet, after 18 hours, and on a diet poor in carbohydrates, after four hours. Control experiments in a healthy subject gave 12, 8 and 2 hours, respectively.—M. B. G.

ADRENAL insufficiency, Acute—in recurrent fever and malaria; pre-existing tuberculosis in the adrenal glands. Portocalis (A.) Tr. Soc. Medico-Chir. d'Athènes, 1918, Session Feb. 20. J. de Med. Bordeaux, 1918, **89,** 169. Pub. in full, elsewhere; see Endocrin., 1918, **2,** 469.

Cases are described of four soldiers who died, two of recurrent fever and two of malaria, having shown symptoms of acute adrenal insufficiency of the choleriform, algid type. Postmortem examination showed only old pulmonary tubercular lesions and tuberculosis of the ganglia and adrenals. Compare with Endocrin. 1918, **2,** 471, 473, 476., Absts. Nos. 354, 357, 366. —R. G. H.

ADRENAL insufficiency in combatants (Insuffisance surrénale chez le combattant). Carles (J.) J. de Méd. d. Bordeaux, 1918, **89,** 185-88.

Fifteen cases are utilized as a basis for an exposition of the current French views on adrenal insufficiency. The cases were apparently of the same sort described in English as "shell-shock." That the adrenals play an essential part in the symptomatology has not been satisfactorily demonstrated. The therapeutic test in such cases is not convincing.—R. G. H.

(ADRENAL) La línea blanca suprarenal, su produccion y significacion diagnostica (Adrenal white line). Sergent (E.) Medicina Moderna (Havana) 1918, **1**, 19-21.

Reprinted in Spanish translation from Endocrin., 1917, **1**, 18-22.

(ADRENAL) Maladie d'Addison chez un fille de treize ans; mort; autopsy (Addison's disease in a girl of 13; death; autopsy). Comby (J.) Arch. de Méd. des Enf. (Paris.), 1917, **20**, 28. Abstr. Brit. Jour. Child. Dis., 1919, **16**, 62.

The patient had probably been infected by her father, who had died of pulmonary tuberculosis. She presented all the symptoms of Addison's disease, including bronzing of the skin, profound asthenia, arterial hypotension, vomiting and almost sudden death after about two months' illness. The only lesions found post mortem were in the adrenals. The right gland was a mere abscess cavity, and the left was studded with caseous nodules.—M. B. G.

(ADRENIN) Observations of the effects of drugs on the ileo-colic sphincter. Kuroda (M.) J. Pharmacol. and Exp. Ther. (Balt.), 1916, **9**, 187-195.

Adrenin contracts the ileo-colic sphincter while the small intestine is relaxed. Confirms Elliott: Jour. Physiol., 1904, **31**, 157.—F. A. H.

(ADRENIN) On the pharmacology of the ureter. VI. Action of some optic isomers. Macht (I.), J. Pharmacol. and Exp. Ther. (Balt.), 1918, **12**, 255-265.

Laevo-rotatory adrenin stimulated the ureteral contractions and raised the ureteral tonus much more than the racemic variety.—F. A. H.

(ADRENAL) Sobre la formula leucocitaria en la enfermedad Addison (Leucocytic formula in Addison's Disease). Marañón (G.) Boletin de la Soc. Española de Biol., Session Dec. 17, 1915.

The blood picture was studied in 13 cases of Addison's disease. One showed leucopenia (4,200), 5 were normal (5-8,000), 3 showed slight hyperleucocytosis (9-13,000) and one marked (30,100). In 3 cases the total number of leucocytes was not determined. As to mononuclear cells, three showed 35-40%; six, 40-50%, and four, 50-60%. There was no apparent relation between the mononucleosis and the severity of the symptoms. Generally the mononucleosis was at the expense of the lymphocytes, but in certain cases there was an absolute augmentation of the large mononuclears. No abnormality in the number of the eosinophiles was detected, nor any abnormal cells in the blood.—R. G. H.

(ADRENALS) Des rapports entre la sécrétion surrénale et la fonction vaso-motrice du nerf splanchnique (Relation between adrenal secretion and the vasomotor function of the splanchnic). Gley (E.) et Quinquaud (A.) C. R. Acad. Sc. (Paris.), 1916, **162,** 86-88.

The rise of the blood pressure upon stimulation of the splanchnic nerve is a purely neuro-muscular phenomenon and the secretion of the adrenals has no part in it, since excitation of this nerve does not lose its effect even in the absence of the adrenals. If the veins of both adrenals are ligated and great care is taken not to injure the fibres of the splanchnic nerve—to carry out which is particularly difficult in the dog—the blood pressure will rise upon stimulation of the splanchnic to the same level as before operation. In order to make sure that no adrenalin was escaping into the circulation through the thoracic duct, the latter also was ligated.—E. U.

ADRENALS, Development of the—in the cat (Sur la development des capsules surrénales du chat. Notes d'organogenèse et de cytogenèse). da Costa (A. C.) Bull Soc. portugaise des sci. nat. (Lisbon) 1916, **7,** 161-71.

A detailed description of the adrenals in cat embryos. From histological evidence it is suggested that adrenin is produced in the latter half of gestation. Physiol. Abst., **3,** 265.

(ADRENALS) Een geval van ziekte van Addisonii (A case of Addison's Disease). Hekman (J.) Nederl. Tijdschr. v. Geneesk. (Amsterdam) 1916, **60,** (ii) 371-72.

Description of a case with pigmentation of the skin, but not of the mucous membrane. Blood sugar and blood pressure were normal. According to the description, the case is not properly diagnosed.—J. K.

ADRENALS, Secretory innervation of the—(Über die sekretorische Innervation der Nebennieren). Popielski (L.) Arch. f. d. ges. Physiol., 1918, **170**, 245-59.

The author believes that the existence of secretory fibres to the adrenals has not been proved—that positive results of reported experiments are due to manipulation of the glands or asphyxia of the medullary portion. The splanchnic fibres to the medulla are vasodilator hence their stimulation leads to flushing out formed adrenin. In experiments in which the amount of adrenin in the two glands was estimated, and in which the nerve was divided on one side so that the denervated gland could serve as a control retention of adrenin in that side was due to resulting anemia. Anemia, nevertheless, results in liberation of adrenin from the complex precursor in which it is present in the gland so that stimulation of the splanchnic results in the passage of large amounts of it into the circulation. The liberation of adrenin in asphyxia is also due to its being set free by the action of CO_2. Manipulation of the adrenal liberates adrenin, but it does not pass from a denervated gland into the circulation until the gland is flushed out with blood, as by stimulating the splanchnic. Physiol. Abst., **3**, 265.

ADRENALS, Sudden post-operative death and tuberculosis of the—(Mort subite post-opératoire et tuberculose des surrénales). Brindeau (A.) Arch. mens. d'Obstét. et de Gyn. (Paris) 1917, **6**, 159-68.

A woman suddenly died after a short, uneventful operation under general anesthesia. At autopsy the adrenal glands were found tuberculous. The author accounts for the otherwise inexplicable death as due to "insuffisance surrénale." Unlike most papers on this topic, this one presents some tangible, specific evidence. The author believes that when a pre-operative diagnosis of such insufficiency can be made (as by the "white line" associated with low blood pressure), local anesthesia should be used or, in case this is impossible, the patient should be fortified by the administration of adrenin.—R. G. H.

(ADRENALS) Sul meccanismo d'azione del cloroformio. II. Azione sulle capsule surrenali. Aloi (V.) Riforma Med. (Naples) 1918, **34**, 990-91.

Experiments were made on dogs. These were subjected to chloroform inhalation for varying periods and at intervals of two or three days. The adrenin content of the adrenal glands was determined colorometrically. It was found that the in-

toxication resulted in a depletion of the glands such as Elliott has described after etherization.—R. G. H.

(ADRENALS) The experimental production of lesions, erosions and acute ulcers in rabbits by repeated injections of pilocarpin and adrenalin. Friedman (G. A.) Jour. Med. Research (Boston), 1918, **38**, 449.

Friedman summarizes his work as follows: The production of gastric and duodenal ulcer will depend upon the synergetic work of vagotrope and sympathicotrope hormones, as in rabbits after repeated injections of pilocarpin and adrenalin. If hormones act independently, either gastric or duodenal ulcers will develop, as occurred in rabbits which were injected with pilocarpin or thyroid and in dogs with adrenalin injections. Since vagotonic and sympathicotonic symptoms and signs are found in the majority of patients afflicted with peptic ulcer, there may exist in such individuals minor degrees of hypertonicity of vagus and sympathicus—the conditions resembling Graves' disease, with the difference, however, that in the latter the hypertonicity of the vagus and sympathicus is likely to be marked. The work of Adler is cited as indicating that the adrenals are disturbed in Graves' disease.—J. P. S.

ADRENALS, The function of the—(La fonction des surrénales). Gley (E.) et Quinquaud (A.) Archives neerlandaises de physiologie de l'homme et des animaux (The Hague), 1918, **3**, 1.

Data published elsewhere. See Endocrin., 1918, **2**, 473.

(ADRENALS) (a) The reactions of the melanophores of the horned toad. (b) The co-ordination of the melanophore reactions of the horned toad. Redfield (A. C.) Proc. Nat'l Acad. Sci. (Washington), 1917, **3**, 202-3; 204-5.

The pigment cells of the horned toad are under reflex and hormone control. That the hormone is adrenin is indicated by the facts that: (1) Adrenin in minute doses causes contraction of the melanophore pigment. (2) The adrenal glands give a substance pharmacologically like adrenin which causes the pigment cells to contract. (3) Faradic stimulation of the adrenals causes a similar reaction. (4) The occurrence of "emotional" hyperglycemia in the horned toad indicates adrenin is secreted during nervous excitement. (5) The melanophore pigment is contracted under the influence of asphyxia, ether, mor-

phia and nicotine. (6) Removing the adrenals blocks the reaction of the melanophores so that (especially in denervated areas) no contraction of the pigment accompanies nervous excitement.—R. G. H.

(ADRENIN) Acción de la adrenalina en la fatiga muscular del Leptodactylus ocellatus (L.) Gir. y. del Bufo marinus (L. Schneid). **(Action of adrenin on muscular fatigue in L. ocellatus and B. marinus.)** Guglielmetti (G.) Rev. Assoc. Méd. Argentina (Buenos Aires) 1918, **29,** 774.

The observations of Dessy and of Grandis are confirmed and extended. Guglielmetti employed adrenin and not suprarenal extract as did the former authors. In general adrenin did not affect the normal muscle, but restored the fatigued muscle, increasing its contractile powers. The original report should be consulted for numerous details. The frog Leptodactylus ocellatus is five times more sensitive than the toad Bufo marinus. (See article by Gruber in this number.)—B. A. H.

ADRENIN, Action of—on the secretion of sweat. Dieden (H.) Ztschr. f. Biol. (München), 1916, **66,** 387-90.

Injection of adrenin into the pad of a cat's paw causes secretion of sweat only after section of the sciatic nerve, unless the animal is deeply anesthetized, in which case section of the nerve is unnecessary. A positive reaction is also obtained six days after division of both sciatics and ten minutes after death. Intravenous injections or subcutaneous injections in other regions are ineffective. The author believes that the sciatic carries inhibitory fibres to the sweat glands which are stimulated reflexly or by adrenin acting on an inhibitory center in the spinal cord. After cutting the posterior roots (containing the inhibitory fibres) in the lower dorsal and lumbar regions, the sciatic remaining intact, adrenin evokes sweating in the hind paws but not the front. Stimulation of the posterior roots now appears to cause the sweat to dry up. Physiol. Abst., **1,** 174.

(ADRENIN) A note on the effect of asphyxia and afferent stimulation on adrenal secretion. Cannon (W. B.) Science (N. Y.) 1917, **45,** 463.

The "splanchnic area" is isolated by tying off carotids, subclavians and aorta above the inferior mesenteric. Blood pressure readings were taken from the proximal end of the

carotid. Any changes in blood pressure were thus due to vascular changes in this area. Asphyxia for one minute causes marked rise, but no result if the adrenals are removed. If the adrenals are denervated there is a longer latent period.

The heart was completely denervated and used as an "adrenalin indicator." Stimulation of central end of a cut sciatic causes an increase in heart rate (50 per min.). The effect is lost if the adrenals are removed or denervated. The effect of asphyxia is not so marked.

A caution is given regarding the manipulation of abdominal viscera with an attendant secretion of adrenalin, confusing the results.—W. E. B.

(ADRENIN) A respiratory factor in the production of adrenin pulmonary oedema in the rabbit. Gates (F. L.) and Auer (J.) J. Pharm. & Exp. Ther. (Balt.), 1917, **9**, 361-2.

Artificial respiration in vagotomized rabbits, with chests intact, greatly reduces the pulmonary oedema produced by adrenin injected intratracheally. Experimentally induced tracheal stenosis, with vagi intact, favors the production of oedema after the intratracheal injection of adrenin. These facts, together with the observation that adrenin causes a definite broncho-constriction in vagotomized rabbits, were explained by the view that the alveoli supplied by a constricted bronchiole act like miniature dry cups, and since there is also pulmonary congestion, the passage of a transudate into the alveoli is facilitated. Artificial respiration prevents the oedema by setting up a positive pressure in the lung.—L. G. K.

(ADRENIN) Arsphenamin and neoarsphenamin plus epinephrin. Beeson (B. B.) Am. J. Syph. (St. Louis), 1919, **3**, 129-38.

In a series of 500 intravenous injections of arsphenamin approximately 3 per cent developed nitroid crises. These varied in manifestation from slight flushing of the face and feeling of precordial fullness to extreme flushing and marked air hunger with edema of tongue and lips and injection of the conjunctiva. In three cases marked prostration occurred. Adrenin, 1-2 milligrams, given intramuscularly ten minutes before the injection, proved beneficial in warding off these ill

effects. Beeson's conclusion that the crises are due to adrenal insufficiency is not justified by the evidence presented.
—R. G. H.

(ADRENIN) Drei Vorschlage zur Namensgebung und schreiben (Three proposed improvements in terminology). Kahn (R. H.) Zentralbl. f. Physiol. (Leipzig) 1917, **32,** 285-90.

One of the proposed changes is "sympathikotropine," or sympathizine for adrenin. Physiol. Abst. **3,** 307.

ADRENIN in asthma. Triviño (G.) Revista Ibero-Americana (Madrid), 1918, **39,** 271-77.

Triviño has used epinephrin in twenty-two cases of asthma and, with one exception, the results were highly encouraging. In this one exception, there may have been a complicating emphysema. In other cases the patients were always relieved within twenty minutes. He followed the technic advised by A. Hertz, who has had considerable clinical experience besides his experience with asthma in his own person. He found that injection of 3 drops of the usual 1 per thousand solution of epinephrin gave prompt relief, but the by-effects were disagreeable. Reducing the dose to 2 drops or even 1 drop proved usually efficient without the by-effects. Triviño did not find the relief so immediate as others have reported, but it was always experienced within twenty minutes.—Jour. A. M. A.

(ADRENIN) Mechanism and control of fibrillation in the mammalian heart. MacWilliam (J. A.) Proc. Roy. Soc. London (1918), **90B,** 302-23.

The paper is mainly physiological. The control of ventricular fibrillation by means of certain compounds ($SrCl_2$, urethan, adrenaline, hirudin, and pilocarpine) is described. Chem. Abst., **13,** 34.

(ADRENIN) On certain antagonists of pilocarpine. Ransom (F.), J. Pharm. & Exp. Therap. (Balt.), 1917, **10,** 169-184.

The only point of endocrine interest is that adrenin very effectively antagonizes the action of pilocarpine on the rate and on the systole of the frog's heart.—L. G. K.

(ADRENIN) PURPURA. Johannessen (C.), Norsk Magazin for Laegevidenskaben (Christiania), 1918, **79,** 1209-52 (Abst. J. Am. M. Assn., 1919, **72,** 318).

In connection with an extensive article on the symptomatology, etiology and treatment of purpura the author discusses the use of adrenin. It is valuable, he says, to arrest the paralysis of the contractile elements of the sympathetic nerve terminals, which is a feature of anaphylactoid purpura. From 0.1 to 0.3 c.c. of the 1 per thousand solution can be injected subcutaneously several times a day. It is ineffectual by the mouth. Administration of epinephrin conforms also to Friedrichsen's theory of the nature of purpura. With abdominal purpura the colic pains may be agonizing. Dieting does not help and warm applications give little relief. Atropin paralyzes the irritated terminals of the vagus nerve in the intestines and thus has a sedative action. He gives it by the mouth or subcutaneously in a 1 per thousand solution.—R. G. H.

(ADRENIN) Quantitative experiments on the liberation of epinephrin from the adrenals after section of their nerves, with special reference to the question of the indispensability of epinephrin for the organism. Stewart (G. N.) and Rogoff (J. M.), Jour. Pharm. Exp. Ther. (Balt.), 1917, 10, 1-48.

See Endocrin. 1917, **1,** 341-2.—L. G. K.

ADRENIN, Synthetic —. Nagayoshi Nagai. Brit. 118,298, July 13, 1917.

Adrenin is obtained by the following synthesis: (1) Diacetylprotocatechuic aldehyde, prepd. by the reaction of AcCl or Ac_2O on protocatechuic aldehyde, is condensed with nitromethane in the presence of weak inorg. or org. bases; (2) the resulting diacetyldihydroxyphenylnitroethanol is reduced in the presence of HCHO by means of Zn dust and HOAc; (3) the diacetyladrenin so formed is hydrolyzed by HCl, giving adrenin hydrochloride. Chem. Abst., **13,** 59.

(ADRENIN) Test glycemia. Loeper (M.) and Verpy (G.) Arch. de. méd et de pharm. militaire (Paris) 1917, **67,** 817.

Adrenin may be used as a means of determining the power of the liver to transform glycogen into sugar. Normal individuals show a rise of 0.40 gm. of blood-sugar one hour after the injection of 1 mg. of active adrenin. This is taken as a standard. In cases of acute irritation of the liver, the rise of blood-

sugar is exaggerated, while, in cases of defective liver action, the reverse is true. Physiol. Abst., **3,** 182.

(ADRENIN) The action of some optic isomers on the ureter. Macht (D. I.). J. Pharm. & Exp. Therap. (Balt.), 1917, **9,** 351.

The only point of endocrine interest is that laevo-adrenin is more stimulating than the synthetic adrenin.—L. G. K.

(ADRENIN) The administration of epinephrin by intraspinal injections in acute or subchronic cases, accompanied by a low blood pressure. Auer (J.) and Meltzer (S. J.) J. Am. M. Assn. (Chgo.), 1918, **70,** 70.

A former observation was corroborated in case of three monkeys in which intraspinal injections of adrenin caused prolonged elevation of blood pressure. This effect persists for an hour as contrasted with a few minutes as a maximum when the drug is given intravenously. The suggestion is offered that 3 c.c. doses of 1:1,000 solution of adrenin intraspinally might be beneficial in clinical cases of low blood pressure. This dosage is regarded as safe.—R. G. H.

(ADRENIN) The coördination of chromatophores by hormones. Redfield (A. C.) Science (N. Y.) 1916, N. S. **43,** 580-81.

The melanophores of the horned toad become contracted during states of nervous excitement. All attempts to prevent the reaction locally by cutting nerves have failed, hence it seems to be due to a hormone. If the circulation to a leg is blocked the melanophores remain expanded, the skin appearing much darker than that of the rest of the body. Removing the blocking ligature causes contraction of the melanophores. The effects in the ligated leg are not due to asphyxia therein. Blood from a horned toad in a state of nervous excitement injected into a lymph space of a second animal causes local paleness; blood from a quiet animal does not have this effect. Hence excitement causes the appearance in the blood of some chemical substance identical with, or similar to, adrenin. Other experiments, later reported, indicate that it actually is adrenin.

—R. G. H.

(ADRENIN) The influence of asphyxia upon the rate of liberation of epinephrin from the adrenals. Stewart (G. N.) and Rogoff (J. M.), Jour. Pharm. & Exp. Ther. (Balt.), 1917, **10,** 49-72.

No increase was detected in the rate of liberation of epinephrin from the adrenals during asphyxia, as determined by testing adrenal vein blood on rabbit intestine and uterus segments. Therefore such phenomena as hyperglucemia and glycosuria when associated with asphyxia, are not due to increased liberation of adrenin from the adrenal glands.

—L. G. K.

(ADRENIN) The influence of ether anaesthesia, of hemorrhage, and of plethora from transfusion on the pressor effect of minute quantities of epinephrine. Rous (P.) and Wilson (G. W.) Jour. Exp. Med. (Balt.), 1919, **29**, 173.

Ether anesthesia has a marked influence in diminishing the pressor response to minute amounts of epinephrine injected directly into the circulation. Hemorrhage acts in much the same way. In plethoric animals the response to small doses of epinephrine is lessened in proportion as the blood pressure is increased by the plethora. In the exsanguinated animal an amount of epinephrine three or four times that sufficient to produce a pressure rise of 10 to 15 mm. of mercury under normal conditions, may be entirely without effect. On the other hand, the response to large doses is uninfluenced by ether or hemorrhage. Hence, if epinephrine is to be used to tide over collapse it should be appreciated that the amount of epinephrine which will suffice under normal conditions to bring up the blood pressure may have little or no effect on an etherized individual or one that has lost blood.—H. W.

(ADRENIN) The mechanism of ether hyperglucemia. Keeton (R. W.) and Ross (E. L.), Am. J. Physiol., (Boston) 1919, **48**, 146-160.

The authors show that a persistent hyperglucemia occurs in normal dogs under continuous ether insufflation. This reaches a maximum at the end of two hours, with little change in the third hour. A transient hyperglucemia passing off at the end of two hours occurs in animals with splanchnic nerves sectioned on both sides. Asphyxia was suggested as the cause of this through an altered reaction of the blood. A persistent hyperglucemia of a lower grade occurs in animals unilaterally splanchnicotomized. Denervation of the hepatic artery does not affect the hyperglucemia. Section of all the nerves in the hepatic pedicle with cauterization of the coats of the hepatic artery, portal vein and common duct prevents the sugar rise from reaching as high a point as in normal dogs, but does not

abolish it. Eck fistula retards the appearance of hyperglucemia in the systemic veins. Ligation of the hepatic artery in Eck fistula animals causes a terminal hyperglucemia. Reversed Eck fistula does not influence the course of ether hyperglucemia. The adrenin content of the suprarenal glands of dogs whose splanchnic nerves had been previously sectioned on one side was found to be unequal in the two glands, although the inequality was not constant (sometimes the denervated gland contained more adrenin, sometimes the control gland, and in other animals there was little difference). However, the authors believe that adrenin is an essential factor in the production of ether hyperglucemia, particularly the persistent type lasting for several hours. The adrenin is believed to act by stimulating the endings of the hepatic splanchnic nerves.

—L. G. K.

(ADRENIN) The output of epinephrine in shock. Stewart (G. N.) and Rogoff (J. M.) Am. Jour. Physiol. (Balt.), 1919, **48,** 22-44.

The authors found that the rate of output of epinephrin in dogs and cats, after the blood pressure had been permanently lowered by exposure and manipulation of the intestine, by partial occlusion of the inferior vena cava, by hemorrhage and by "peptone" injection, was the same as before the lowering of the blood pressure, within the limits of error of the methods (rabbit intestine and rabbit uterus segments) used for assaying the epinephrin. A marked increase in the rate of output of epinephrine was produced by strychnine, probably due to its stimulating action on the epinephrin centre in the lower thoracic cord.—L. G. K.

(ADRENIN) Über die Henlesche Chromreaktion der sogenannten chromaffinen Zellen und den microchemischen Nachweis des Adrenalins. Ogata (T.) and Ogata (A.) Mitt. a. d. Med. Fak. d. k. Univ., Tokyo, 1917, **17,** 173-85.

Published elsewhere. See Endocrin., 1917, **1,** 349.

(ADRENIN, THYROID) Glucemia é hiperglucemia adrenalinica en la paloma (Glucemia and adrenin hyperglucemia in the dove). Marañón (G.) and Rosique (A.) Boletin Soc. Española de Biol. 1916, Session, June 10.

Analysis by Bang's method gave an average glucose content of the blood in normal doves of 0.080 per cent. Adrenin

injections constantly increased the percentage to about 0.09 or 0.10. Treating the doves with thyroid extracts did not augment the adrenin glucemia reaction as it has been reported by several observers to increase the vasomotor effects.—R. G. H.

A SEX—intergrade strain of Cladocera. Banta (A. M.) Proc. Soc. Exp. Biol. & Med. (N. Y.), 1916, **14**, 3-4.

The older conception was that sex is an absolute attribute. An organism was supposed to be either a male or a female except in rare cases of hermaphroditism. Researches of recent years have shown, however, that the blending of "maleness" and "femaleness" in a single individual is not uncommon.

Banta studied a race of Cladocera which for 130 generations had been breeding parthenogenetically, none but females appearing. In the 131st generation males and sex-intergrades of many sorts appeared. In the species studied eight morphologic secondary sex characters are recognized. Practically every possible combination of male and female characters was seen. The gradation ran from normal females, females with a few male characteristics through hermaphrodites with various combinations of sex characters to male intergrades and finally complete males.

Various anomalous individuals seen by clinicians are probably true sex intergrades.—R. G. H.

(CARBOHYDRATE METABOLISM) Metabolism of glucose in surviving organs. Lombroso (U.) and Artom (C.), Arch. farm. sper. (Rome) 1917, **24**, 215-22, 223-30, 263-7, 268-79.

Circulation of Ringer's solution plus glucose through the liver of a dog which had fasted several days does not result in loss of carbohydrate. But the liver from a nourished dog destroys some of the glucose, as do also intestine, spleen and pancreas. (See also Endocrin. 1917, **1**, 357.) Physiol. Abst. **3**, 318.

CATALASE ACCELERATOR, Does the liver secrete a—? Burnett (T. C.) Proc. Soc. Exp. Biol. & Med. (N. Y.), 1918, **15**, 80.

Published elsewhere. See Endocrin. 1918, **2**, 328.

(CORPUS LUTEUM) Les variations de la cholésterinémie durant le cycle menstruel (D'après des recherches recents) (Variations in cholesterinemia during the menstrual cycle,

according to recent researches). Chauffard (A.) Presse méd. (Paris), 1917, **25,** 329-31.

Recent experiments seem to establish as a fact that the corpus luteum is a gland of internal secretion not only histologically, but also in its function, and that at least one of the substances manufactured by this gland is cholesterine. Chauffard, in 1911 and 1912 demonstrated the presence of cholesterine in the corpus luteum of the menstruation period and a cholesterinemia prevailing during pregnancy; the corpus luteum is a center for the production of cholesterine. G. P. Goñalons (Semana Medica No. 51, Buenos Aires, 1916) reports 27 determinations of the cholesterine content of the blood each one comprising a complete period; a periodic hypercholesterinemia exists, beginning several days before and ending 3 to 4 days after menstruation (total duration of 11 to 13 days), and comprising two maxima, one before and one during menstruation. In three cases where menstruation did not take place for pathologic reasons, a periodic cycle of hypercholesterinemia corresponding to that in normal menstruation, was nevertheless observed; the corpus luteum is not the only center of cholesterine production. C. concludes that the peculiar frequency of gall stones (cholesterine concretions) in women is due to the presence in the gall bladder of an excess of cholesterine during each menstruation resulting from the hypercholesterinemia.—E. U.

CORPUS LUTEUM, Soluble extract of—used in the vomiting of pregnancy. Zimmerman (B. F.) Louisville Monthly J. Med. & Surg., 1916, **23,** 129-30.

Reports brilliant results in a stubborn case which had not been benefitted by desiccated corpus luteum, opium and hyocyamus or chloral. Five injections only of the soluble extract (1 c.c. each) were required.—R. G. H.

(DIABETES) (1) Blutzucker und Rest Kohlenstoff beim Diabetes mellitus des Menschen. (2) Die Vertheilung des Blutzuckers auf Körperchen und Plasma beim menschlichen Diabetes. [(1) Blood sugar and residual carbon in human diabetes. (2) Distribution of blood sugar between corpuscles and plasma in human diabetes.] Stepp (W.) Deutsch. Arch. f. klin Med. (Leipzig) 1917, **124,** 177-98; 199-206.

In some cases hyperglucemia accounts for extra residual carbon in the blood, i.e.: carbon not precipitated by phosphotungstic acid. But in most diabetics this carbon is less than that

expected from the extra sugar, and in some cases it is higher. This suggests that in the majority of cases there are reducing substances in the blood with a lower carbon content than glucose, and among those found are glycol aldehyde, glyceric aldehyde and dioxyacetone. In cases where the residual carbon is higher than that calculated from the sugar there must be an increase of non-reducing carbon compounds. In experimental diabetes with phloridzin (1 case) the residual carbon was unexpectedly low; in pancreatic diabetes it is higher. (2) In 12 cases the sugar percentage in the plasma was higher than in the whole blood; in three cases the converse was found; in one case the two were equal. In experimental (phloridzin and pancreatic) diabetes the plasma sugar percentage was the higher. Physiol. Abst. **3,** 248.

DIABETES, Calcium soap deposit in the liver during—. Hagiwara (R.), Iji Shimbun, 1917, **981,** 1201-2; Jap. Med. Literature (1918), **3,** 62.

At the autopsy of a patient who had shown acetonuria, deposits of Ca soaps were found in the liver such as occur in fat necrosis as a result of pancreatic lesions. No lesion could be demonstrated in the latter organ, and no explanation could be found for the deposits. Chem. Absts., **13,** 475.

DIABETES, Clinical aspects of the fasting treatment of—. Rowe (A. H.) Calif. State J. Med. (San Francisco), 1918, **16,** 433-38.

An excellent brief exposition of the practical features of the fasting treatment together with tabular analysis of 40 cases, giving extensive laboratory findings.—R. G. H.

(DIABETES) Hyaline degeneration of the islands of Langerhans in pancreatic diabetes. Winternitz (M. C.) Johns Hopk. Hosp. Rep. (Balt.), 1916, **18,** 37-48.

A detailed microscopic study of the pancreas of a man who had had mild diabetes mellitus for 18 or more years. Both interacinar fibrosis and marked hyaline degeneration of the islands of Langerhans were seen. The author remarks that the more recent experimental evidence supports the insular theory of pancreatic diabetes, but it must be borne in mind that the pancreas forms only one link in the chain that controls carbohydrate metabolism. Diabetes may occur when the pancreas is apparently normal, with lesions of the central nervous system

or disturbances in certain endocrine glands. In pancreatic diabetes the important lesion is in the islands; there may be a decrease or an actual increase in size and number of these or a qualitative change. The remarkable power of the insular tissue to regenerate as well as subsequent disappearance of degenerated islands complicates the anatomical interpretation.
—R. G. H.

(DIABETES) Lipoids in one hundred thirty-one diabetic bloods. Gray (H.) Bost. Med. Surg. J., (1917), **178,** 16, 50, 91, 120, 156.

In this long series of articles the results and details are given of many determinations of total fats, total fatty acids, glycerides, cholesterol and phosphatides in 131 diabetic bloods. It is impossible to present the content of all the papers in abstract form. Some of the outstanding points are as follows: There is a lipoid threshold, by Bloor's method, of about 0.7%, analogous to the glucose threshold of 0.1%. Only 7% of diabetics come inside the threshold of the normal Bloor values. The maximal total lipoid value of this series was 16.3%. The higher the lipoids the more unfavorable the prognosis. With acidosis the lipoids are above the level in diabetes without acidosis. Chem. Abst., **12,** 1368.

DIABETES, Metabolism in—, nephritis and cholecystitis. Breed (Lorena M.), Calif. State J. Med. (San Francisco), 1918, **16,** 327-330.

A general discussion with brief reference to several illustrative cases.—R. G. H.

DIABETES, Modern views on—. Poulton (E. P.), Lancet (London), 1918, (i), 863-6, 895-7; (ii), 31-4.

Treatment and acidosis are dealt with chiefly.

DIABETES, Renal—. Bailey (C. V.), Am. J. Med. Sci. (Phila.), 1919, **157,** 236-52.

Two cases are described in detail with results of glucose tests. An interesting discussion of the differentiation between renal and pancreatic diabetes is included.—R. G. H.

(DIABETES) Respiratory exchange and blood sugar regulation. Bernstein (S.) and Falta (W.) Deut. Arch. klin. Med. (1918), **125,** 233-83; Physiol. Abstracts **3,** 245.

On oral administration of carbohydrates the respiratory

quotient rises only when the glycogen reserves of the body are full. On giving sugar intravenously or injecting adrenin, the R. Q. rises whether the glycogen depots are full or not. Injections of pituitrin lessen heat formation and raise the R. Q., the condition of glycogen reserve making little or no difference.—Chem. Abst., **12,** 2357.

DIABETES, Theory of—. Jacoby (M.) Deutsch. Med. Wchnschr. (Berl.), 1916, **42,** 478-79.

A critical discussion of various views, many of which do not recognize the complex nature of the disordered metabolism which underlies the diabetic state. No new experiments are given, but it is suggested that such questions as the relationship of diabetic muscle to hexose-phosphoric acid and to lactacidogen require investigation.—Physiol. Abst., **1,** 227.

DIABETES, Serum for—. Parke, Davis & Co. Can., 184,763, June 4, 1918.

A serum which decreases blood pressure and increases sugar metabolism is prepared by administering to horses or other suitable animals an extract of the pituitary body and then deriving the serum.—Chem. Abst., **12,** 2411.

DIABETES, The acetone bodies of the blood in—. Kennaway (E. L.) Biochem. J. (Liverpool), 1918, **12,** 120-30.

The concentration of acetone bodies in the blood in diabetic coma may be equivalent, when reckoned as aceto-acetic acid, to that of a 0.03 N solution; this amount is sufficient to combine with more than one-third of the sodium of the plasma. The amounts of aceto-acetic acid show less variation in the series of cases than do those of B-hydroxybutyric acid. Methods for the estimation of acetone and aceto-acetic acid are as a rule tested with acetone only. It is pointed out that this is quite inadequate, as the recovery of aceto-acetic acid is liable to an error which does not occur in the case of either acetone or B-hydroxybutyric acid.—Physiol. Abst., **3,** 319.

DIABETES, The treatment and laboratory control of—. Langstroth (L.) Cal. State J. Med. (San Francisco), 1919, **17,** 5-11.

An exposition of the methods used in the Hospital laboratories of the University of California. Chiefly of technical interest.—R. G. H.

DIABETES INSIPIDUS, Über intramediäre Vorgänge beim— (Metabolism in—.). Veill (W. H.) Biochem. Ztschr. (Berlin), 1919, **61,** 317.

As regards the symptoms, polyuria, polydipsia and dilute urine, diabetes insipidus is a well defined disease. This latter symptom, contrary to frequent statements, is always present, but its degree is remarkably variable even in a single individual. Blood analysis discloses two distinct types of the disease. In one the chlorin in the blood is increased and in the other diminished. The first class cannot retain water and would die without a plentiful supply. This class alone responds favorably to treatment with posterior lobe pituitary extracts. The relation between the internal secretions, the nervous system and diabetes insipidus is unknown. Therapeutic success with pituitary extracts does not prove that the corresponding gland is at fault; it merely proves that the extract influences the tissues, causing them to retain water.—J. K.

DIABETES mellitus and the PANCREAS. Heiberg (K. A.) Nord. med. Ark. (Stockholm), 1918, **50,** 663-80.

Two forms of pancreatic diabetes are distinguished, those in which the injury is confined to the islets of Langerhans, and those in which the ordinary tissue is also involved. Progress of the disease depends on fresh islet degeneration, whereas improvement follows on their regeneration and growth. The islands should be examined quantitatively. In an area of 50 mm. in the tail of the pancreas, 6 out of 75 diabetic cases had 76 to 150 islets, the remaining 69 showed less than 75. In 75 non-diabetic pancreases there were 5 with less than 75 islets, but in the remainder the number was not so high as in diabetic cases. The two groups cannot be correlated with the clinical varieties. Rapidly progressing cases especially in the young, are, however, solely due to islet affection.—Physiol. Abst., **3,** 379.

DIABETES MELLITUS, Dietetic treatment of—. Cammidge (P. J.) Am. Med. (N. Y.) 1918, **13,** 388-401.

Discussion of various diets used in diabetes.—Chem. Abst., **12,** 2352.

ENDOCRINE disorder, uric acid diathesis as an—. (La diatesis urica como un trastorno de secrecion interna). Pita (A.) Medicina Moderna (Havana), 1918, **1,** 31-34.

A theoretical discussion. No specific new evidence is offered.—R. G. H.

(ENDOCRINE GLANDS) An anatomical study of senescence in dogs, with especial reference to the relation of cellular changes of age to tumors. Goodpasture (E. W.), Jour. Med. Research (Boston), 1918, **38,** 127.

This report is based upon a detailed study of 50 dogs. Only that portion dealing with the endocrine glands will be reported. The paper embodies a conception that "With a continued increase in structural intricacy, incident to ageing, the body cells gradually lose their metabolic equilibrium, so that the ultimate conclusion of progressive cell differentiation is death. But . . . it is possible for many cells to return to a more simple form in which special function is absent, or subordinate to growth and division. . . . This process of elimination of structural differences, or metaplasm, is called "dedifferentiation.'" A dedifferentiated cell may differentiate again, reforming structural substances similar to those formerly possessed, and perhaps function normally. But when dedifferentiation has proceeded far enough, under abnormal conditions, a metaplastic transformation may result, the cells producing structural characteristics which they did not formerly have.

There appears to be a greater number of interstitial Leydig's cells in the testicles in old than in middle age. Definite tumors made up of small multinucleated masses of Leydig's cells were not uncommon in the animals studied. The ovaries were usually small, scarred and fibrous. They commonly contained cysts, occasionally corpora lutea, and in two instances macroscopic tumor nodules derived from follicular epithelium which began to proliferate after death of the germinal cells. The adrenals were usually larger than normal and their surface irregular with smooth, more or less spherical protuberances from one to twenty millimeters in diameter, usually multiple and occurring in both glands. There was usually great irregularity in the architecture of the cortex due to combined atrophy and hyperplasia. There were no outspoken degenerative changes in the cells that could be constantly found and followed, but there were indications of a gradual disappearance and replacement of the parenchyma. Indirect evidence of degeneration was the presence to a greater or less extent of phagocytes in the lymph spaces filled with brownish finely granular pigment. Hyperplastic changes of the cortex were found in all three zones. No disintegrative or degenerative changes were found in the medulla.

The parathyroids showed little deviation from the normal. In one instance there was a complete conversion of the gland into a thin walled cyst lined by a single layer of cuboidal epithelium. The thyroid glands in very old dogs were smaller than normal. There was a marked irregularity in the distribution of the colloid. Areas of metaplasia may be present. In three glands multiple cysts were found lined usually by three or four layers of epithelium, with the layer nearest the lumen partially or completely differentiated. In the thymus glands of old animals cysts lined by cuboidal cells were common. Cysts were also seen in the hypophysis.

As the dog grows old, many cells, by dedifferentiation, free themselves of the more rigid demands of functional specificity and become more capable of growth. In the hypophysis, thyroid, thymus, adrenals, testicles and ovaries, as well as in other organs, this power to grow results in tumors. In proportion to the activity of this power of growth, the resultant tumors are benign or malignant.

The tumors found in the endocrine glands of the fifty dogs were:

Tumors Benign and Malignant

Organ	Male	Per Cent	Female	Per Cent	Tot. Per Cent	Malig. nant	Per Cent
Adrenal	29	78	13	100	84	1	2
Hypophysis	1	3	....	....	2	....	....
Ovary	....	....	6	45	....	....	....
Testis	21	63	....	....	63	4	8
Thymus	1	3	....	....	2	....	....
Thyroid	4	12	7	52	22	....	....

—J. P. S.

(ENDOCRINE GLANDS) Recent progress in gynecology. McCann. (F.) Practitioner (Lond.), 1918, **101**, 194. Abst. Surg. Gyn. & Obst., **28**, 160.

A discussion of the endocrine factors in uterine and ovarian functioning. The ovaries, corpus luteum and post-hypophysis exercise control over the uterus and adnexae. There is a definite interaction between ovarian, corpus luteum and menstrual decidua secretions and hypophyseal secretions. Probably dysmenorrhea and pre-menstrual pain are frequently due to excessive activity of the corpus luteum. Menstruation is left in abeyance for the period of pregnancy by the presence in the uterus of the "placental gland." The normal menopause with ovarian retrogression is usually coincident with alterations in the thyroid and hypophysis. Altered ovarian secretion as evi-

denced by menstruation is indicative of altered glandular interaction. Lactation amenorrhea is due to mammary hormone antagonizing the corpus luteum. A persistent thymus is associated with hypoplastic ovaries, while early retrogression of the thymus results in large hyperplastic ovaries. Various other similar statements are made, a conclusive demonstration of which would give scope for many detailed researches.

—R. G. H.

(ENDOCRINE GLANDS) Studies on alimentary hyperglycemia and glycosuria. Bailey (C. V.), Arch. Int. Med. (Chgo.), 1919, **23,** 455.

An interesting paper relative to alimentary glycemia and glycosuria resulting from the ingestion of glucose in weak tea. Following the taking of the glucose, blood and urine specimens were collected at frequent intervals for from six to eight hours. Normal individuals and those suffering from disturbed renal and endocrine function were studied.

Sugar is a constant constituent of normal urine, and, during a fasting and thirsting state, the concentration in the urine approximates that in the blood. In a normal person the sugar in the urine parallels that in the blood up to the latter's concentration of 0.16 to 0.17 per cent. Above this the kidneys actively secrete sugar. In returning to the normal value the decrease in blood sugar precedes that in the urine. Alimentary hyperglycemia is prolonged in myxedema and hypopituitarism. The concentration of blood sugar at which glycuresis occurs varies in different individuals, and is influenced by disease, being abnormally low in early diabetes, high in diabetes of long standing, in nephritis, and in deficiency of the thyroid and hypophysis. Glycuresis is a kidney function and is excessive in diabetes and hyperthyroidism. It is greatly decreased in nephritis and in deficiency of the thyroid or hypophysis. Blood sugar estimations from two to three hours after the ingestion of glucose may be the same in diabetes of long standing, in nephritis, myxedema, or in hypopituitarism.—H. W.

(ENDOCRINE GLANDS) The use of X-rays and electricity in exophthalmic goitre and other disorders of the ductless glands. Hernaman-Johnson (F.), Arch. Radiol. & Electrotherap. (Lond.) 1918, **23,** 91-99.

The author concludes that in exophthalmic goitre X-rays are a specific in the sense that the secretion of the thyroid may be diminished to any required extent. Cure cannot be effected

in the presence of any persistent irritation, and reduced activity of other endocrine glands may delay cure. Bedside administration of X-rays in acute cases is recommended, but in critical cases operation alone offers hope.

In dysmenorrhea of ovarian origin when drug treatment has failed and when there is no gross surgical lesion, a trial should be given to X-rays. The first period may be worse and the second little better, but the third should be unmistakably better. Otherwise the treatment should cease. In young women, complete suppression of ovarian function should not be attempted by X-rays. As regards other endocrine glands X-ray treatment is in its infancy, but progress is predicted. In no class of cases is unintelligent routine treatment less conducive to results than in those mentioned.—R. G. H.

(ENDOCRINE GLANDS) War neuroses, shell shock and nervousness in soldiers. Bailey (P.) J. Am. M. Assn. (Chgo.), 1918, **71,** 2148-53.

Many of the neuroses of the neurasthenic or psychasthenic types are associated with symptoms suggestive of endocrine disturbances and the thyroid picture, especially in gas cases, is much in evidence. Thus in addition to the symptoms of fatigue, lack of confidence, phobias, compulsions and general hyperesthesia, are observed rapid pulse, cardial irritability, pain over the heart, vomiting and terrifying dreams.—Excerpt quoted, p. 2150.

(ENDOCRINE GLANDS) Wirkung von Explosionen auf das menschliche Nervensystem. de Crinis, Arch. f. Psych. (Berlin), 1918, **59,** 988.

After explosions nervous symptoms may occur. The author finds in such cases destruction of adrenal, and often, of liver and pancreas tissue by ferments (Abderhalden), "sympathicotonie" (mydriasis, vasomotor symptoms) and alimentary glycosuria. The intrinsic unreliability of the anamneses and the incomplete clinical descriptions of the cases render the article entirely unconvincing.—J. K.

(ENDOCRINE ORGANS) A therapeutic suggestion concerning endocrines. Bandler (S. W.) Med. Rec. (N. Y.), 1919, **95,** 429-32.

A general article analyzing the action of endocrine factors in practical gynecology. The author includes mammary gland

and placenta extracts among the valuable opotherapeutic products.—R. G. H.

(ENDOCRINE ORGANS) Epilepsy and ductless glands. Prior (G. P. U.) and Jones (S. E.) J. Ment. Sci. (Lond.), 1918, **64**, 30-35.

According to numerous quoted authorities, epileptiform seizures may occur as a result of disease in most of the endocrine organs. These are considered to be concerned in Ca metabolism, and epilepsy is supposed to be due to an upset of Ca metabolism. Numerous cases are cited which, the authors consider, support this view. They appear to have administered extracts of most of the ductless glands without reason and without success and to have performed no original research. —Physiol. Abst., **3**, 386.

(ENDOCRINE ORGANS) Some observations on the effects of feeding glands of internal secretion to chicks.. Wintermitz (M. C.) Johns Hopk. Hosp. Rep. (Balt.), 1916, **18**, 21-23.

Three groups of experiments are summarized:

I. Twenty-two white Leghorn chicks, 11 experimental, 11 control. Fed small doses of powdered dried hypophysis, five months. The experimental animals developed more rapidly and began egg laying earlier than the controls. The differences were striking.

II. A group, number not specified, fed adrenal, hypophysis, ovary, thyroid and thymus (different individuals for each). The only constant result was delayed growth and a condition suggestive of rickets in the thyroid group.

III. Similar to II, including fresh and three sorts of dried hypophysis. No effect except that thyroid interfered with growth. The negative results in the latter experiments are tentatively ascribed to seasonal or other variations in the hypophysis material.—R. G. H.

(ENDOCRINE ORGANS—SYMPATHETIC N. S.) The interdependence of the sympathetic and central nervous systems. Orr (D.) and Rows (R. G.) Brain (London), 1918, **41**, 1-22.

The thesis is elaborated that certain degenerative changes in the spinal cord and brain associated with visceral cancer, Addison's disease, severe anemia and experimental infection of

the peritoneal cavity are traceable to disordered influence of the sympathetic system and endocrine organs. The "protoplasmic neuroglia" is involved as a possible intermediary, and Achûcarro's hypothesis (reviewed Revista di Patologia Nervosa e Mentale, 1917, **22**, 321) that that tissue in addition to a nutritive role secretes "emotional" hormones. But Lugaro's criticism (ibid., 323) is also evaluated. Various facts, chiefly embryological and physiological, are adduced as a priori support for the author's views.—Physiol. Abst., **3**, 420.

(ENDOCRINE ORGANS) The "higher up" theory of sterility in women and its relation to the endocrines. Bandler (S. W.), N. Y. Med. J., 1919, **109**, 309-13.

A general discussion impossible to abstract satisfactorily. Bandler believes that the inability of formed ova to escape leading to "cystic ovaries" and subsequent pressure on other developing ova is an important factor in causing sterility. Rupture of the follicles is also at times prevented by lack of proper hormone stimulation. This is best supplied by ovarian and thyroid extracts. Other stimulants of the genital function are suprarenal and post-pituitary extracts. The menstrual function may be depressed by thymus, mammary and placental extracts and in some phases, probably, by thyroid. The best opotherapeutic results have been obtained in threatened abortion, in which ovarian and thyroid extract and "ovarian residue" with occasional doses of morphine were given.—R. G. H.

(ENDOCRINE ORGANS) The pathogenesis of deficiency disease. McCarrison (R.) Brit. Med. J. (Lond.), 1919, ..., 177-8. (Feb. 15.)

An abstract of a paper to be published in full in the Indian J. Med. Res. The fact that the influence of vitamine deficiency on the endocrine glands has not been carefully studied is unfortunate. McCarrison studied the problem in pigeons fed solely on polished rice. Of these, 168 developed polyneuritis; a large proportion had concurrent septicemia. As controls 72 pigeons were used. It was found that this restricted diet led to functional and degenerative changes in every tissue and organ of the body. The resulting symptomatology was ascribed particularly to chronic inanition, derangement of digestion and assimilation, disordered endocrine function, mal-nutrition of the nervous system and to "hyperadrenalinemia."

The theory of hyperadrenalinemia is deduced from the fact that the adrenals were markedly enlarged and had a greater adrenin content than normal. That this resulted, however, in increase of actual circulating adrenin, no specific evidence is offered; the hypertrophy might conceivably be a "detoxication" reaction. The pituitary in the males showed slight enlargement and the thymus, testes, spleen, ovaries, pancreas, thyroid, etc., were atrophied. Simple inanition gives rise, according to the author, to similar results—a finding not entirely in accordance with Jackson's results in rats. The concurrent edema is ascribed to increased adrenalin production resulting in increased intra-capillary pressure. This theory is opposed by the results of several recent studies of adrenin pharmacology. Among other effects complete ilens would be produced by adrenin in concentration sufficient to cause such capillary constriction.—R. G. H.

ENDOCRINE SYSTEM, Uric acid and the—. Silvestri (T.) Polioclinico (Rome), 1918, **25,** 184. J. Am. Med. Assn., **71,** 608.

The results of S.'s research apparently support his theory that the endocrine-sympathetic system presides over the metabolism in general as a regulator, or physiologic stimulus indispensable for its normal rhythm, but is not the chief factor in the metabolism. It merely stimulates or checks the activity of the metabolism in general, including the production and destruction of uric acid.—Chem. Abst., **12,** 2360.

ENDOCRINOLOGY and opotherapy of shock. Bate (R. A.) Ky. Med. J. (Bowling Green), 1918, **16,** 558.

An article including some speculative endocrinology emphasizing the usefulness of pituitrin injections in shock.
—R. G. H.

GIGANTISM (acromegalic) associated with bilateral, symmetrical syndactylism of the second and third toes (Gigantismo acromegalico associato a sindattilia simmetrica bilaterale del secondo e terzo dito del piede). Battistini (F.) Riv. crit. di Clin. Med. (Firenze), 1916, **17,** 185-8.

A case is described and theorized upon to the effect that the condition was due to fetal dyspituitarism.—R. G. H.

(GONADS) De l' influence des extraits de glandes génitales sur le métabolisme phosphoré (Influence of gonad extracts on phosphorus metabolism). Jean. C. R. Acad. Sc. (Paris), 1917, **164**, 438-40.

Extracts of the interstitial tissue of the testicle and of the active corpus luteum cause a distinct decrease of phosphoric acid excretion. The interstitial tissue of pig's testicles and the active corpora lutea of pig's ovaries were extracted in physiological serum and the extracts administered by injection to male and female nurses respectively. The excretion of phosphoric acid in urine and feces after injection was compared with the excretion before injection, the diet having been the same before and after injection; the amount excreted after injection was considerably smaller than that before injection. It was noted also that injection of corpus luteum extract was followed after from 2 to 3 days, by hypertrophy of the mammary glands.—E. U.

GONADS, Endocrine function of the—and heredity (Over die inwendige afscheiding der geslachtsklieren en de erfelykheidsleer). Vermeulen (H. A.) Tijdschr. v. Diergeneesk. (Utrecht), 1917, **44**, 681-91.

A general discussion presenting no new data.—J. K.

(GONADS) Eunuchoidismus. Fischer. Deutsche Med. Wchnschr. (Berlin), 1916, **42**, 214.

Demonstration of three cases:

(a) Individual was tall with atrophic genitals and skiagram showed a large sella turcica.

(b) Individual was very fat with atrophic genitals and a small sella turcica.

(c) A girl of 16, very small, with small sella, atrophic uterus and much fat in the breasts.

In each case 400 gms. of glucose failed to cause glycosuria.—J. K.

(GONADS). Goodale's experiments on gonadectomy of fowls. Morgan (T. H.) Science (N. Y.) 1917, **45**, 483. [Referring to Gonadectomy in relation to secondary sexual characters of some domestic birds. Goodale, Carnegie Inst., (Wash.), 1918, No. 243.]

Rouen ducks and brown Leghorns were employed. Removal of testes showed inconclusive results, although chiefly

negative. Removal of ovary was difficult, but when successful the duck and hen assumed male plumage. Ovaries transplanted into a castrated cock prevented the assumption of characteristic male plumage. Spurs develop in capons as well as cocks, and in all spayed females (brown Leghorn). The spur develops normally in some females.

Inconclusive data with reference to voice characteristics are offered.

Goodale submits the theory that the internal secretion of the ovary is a "simple" substance inhibitory in action. It prevents the appearance in the female of the male characteristics, which are inherited equally by both sexes, the nature of the reaction simulating an oxidation process.

The discussion is closed with an intimation that the process is probably not so simple, but composed of a series of successive reactions.—W. E. B.

(GONADS) La courbe myo-glycérinique. (Glycerine muscle curve.) Rocha (A. D'A.) Bull de la Soc. Portug. des Sci. Nat. (Lisbon), 1917, **8,** 1-22. Physiol. Abst. **3,** 228.

It was noted that the effects of drugs on frog's muscle curves varies with the sexual cycle of the animals. This indicates that sex hormones play a part in controlling muscular activity. The paper is mostly concerned with the effect of glycerine on muscle.—R. G. H.

GLYCOSURIA, Study of an unusual—. Langstroth (L.), Am. J. Med. Sci. (Phila.), 1919, **157,** 201-205.

A case of glycosuria with apparently lowered renal threshold for glucose is reported with details as to blood and urine findings. The blood sugar curve showed a higher rise than normal and a delayed fall such as has been found associated with mild diabetes and other endocrine diseases. This is evidence of abnormal carbohydrate metabolism. True diabetes was probably not present.—R. G. H.

(HORMONES) Chemical correlation in the growth of plants. Baylis (W. M.) Nature (Lond.), 1918, **102,** 285-7.

A review of experimental work on the chemical basis of regeneration and geotropism in plants (Botan. Gazette, 1915, **60,** 249; 1917, **63,** 25; 1918, **65,** 150; Science, 1917, **66,** 115, 547; Proc. Nat. Acad. Sci., 1918, **4,** 117). The greater growth of the apical buds of plants as compared with the lateral buds of the stem is explained on the assumption that when the leaves

are first removed inhibitory substances are present everywhere throughout the stem, but that these have a tendency to flow towards the base. Hence the most apical node is the first one to become freed from their presence, and when its buds grow they form anew the inhibitory substance which prevents the growth of the more basal buds. Evidence is offered that the inhibitory effect is proportional to the size of the growing apical bud.—Chem. Abst., **13,** 613.

(HYPOPHYSIS) Acromegaly, A case of—in a child (Een geval van reurengroei bij een kind). de Monchy (L. B.) Nederl. Tijdschr. v. Geneesk. (Amsterdam), 1916, **60** (i) 597.

Description of a case in a child of 17 months. There was no goitre or symptoms of hypophyseal tumor. Glycosuria could not be produced either by injections of adrenin or administration of glucose.—J. K.

(HYPOPHYSIS) Acromegaly of long standing without subjective symptoms. Williamson (C. S.) Med. Clin. Chicago, 1916, **1,** 885-893.

Report of a case of acromegaly with typical objective symptoms— marked prognathism, enlargement of the nose and increase in size of the extremities—without any of the usual subjective symptoms. The patient was a man thirty years old. The precise manner in which the disease began escaped his notice. The present condition of his features and extremities has been almost unchanged for the past twelve years; but during this time he has grown 5 or 6 inches in height and gained 90 pounds in weight. There was nothing of importance in the family history. A Roentgenogram revealed an enlargement of the sella turcica.—J. P. S.

The HYPOPHYSIS and hypophyseal disease. Schnoor (E. W.) J. Mich. State Med. Soc. (Grand Rapids) 1919, **18,** 87-96.

A general review of the more significant literature. No original data.—R. G. H.

(HYPOPHYSIS) Case of dyspituitarism in a girl aet. 15 years. Stephenson (S.) Proc. Roy. Soc. Med. (Sect. Stud. Dis. Child.) (Lond.), 1915-16, **9,** 23-26.

Published elsewhere. See Endocrin., 1918, **2,** 64.

(HYPOPHYSIS) Case of mental imbecility and absence of sella turcica; improvement by organotherapy. Leiner (J. H.) N. Y. Med. J., 1919, **109,** 156-7.

An interesting case resembling Lorain hypophyseal infantilism in a girl of 12. The cranial skiagram indicated absence of sella turcica. The patient had a mentality of about four years (Binet-Simon scale). She was timorous and irritable. The shafts of the long bones were elongated; premature ossification of the epiphyses was apparent in skiagrams and prognathism was obvious. Low blood pressure and asthenia were marked. Menstruation had not appeared. The thyroid was not palpable and no evidence of thymus hyperplasia was elicited. Sugar assimilation was below normal. Treatment with thyroid and thymus preparations was inefficacious, but persistent administration resulted in marked increase in weight and strength and, within three months, in a mental advancement of three years.—R. G. H.

(HYPOPHYSIS) Congenitalen Akromegalen habitus, Een geval van familaren—. Scheffer (C. W.) Psych. en neurol. Blad. (Amsterdam) 1917, **21**, 211-18.

Description of a case in a family of which two brothers and a sister had typical acromegaly.—J. K.

(HYPOPHYSIS) Diabete insipido da emorragia nelle neuroipofisi e nel peduncolo ipofisario (Diabetes insipidus from hemorrhage in the neurohypophysis and into the pedicle). Luzzatto (A. M.) Lo Sperim. (Firenze) 1918, **71**, 405.

In man the syndrome of diabetes insipidus may arise from destructive lesions of the neurohypophysis or its pedicle even though there occurs no apparent injury to the adjacent infundibular region. These lesions may be accompanied by severe cachexia similar to that produced experimentally by section of the pedicle or by total hypophysectomy. Hemorrhage may occur spontaneously in the neurohypophysis and produce morphological changes like those produced by hemorrhage in any other parts of the central nervous system. Consequently, hemorrhage must be considered as a possible etiological factor in the so-called spontaneous cases of hypophyseal disorder.
—A. L. T.

(HYPOPHYSIS) DIABETES INSIPIDUS, treatment of—with pituitary extract. Rosenfeld (G.) Berlin klin. Wchnschr., 1916, **53**, 553-55.

See Endocrin., 1917, **1**, 272.

(HYPOPHYSIS) Dyspituitarism; Report of cases of disorder of the pituitary gland, occurring in the pre-adolescent period, and differing widely in clinical manifestations. Moleen (G. A.) Arch. of Diag. (N. Y.) 1917, **10,** 103-122.

Four cases are described, illustrated with photographs.

Case I. Male, age 26: Pre-adolescent dyspituitarism with optic atrophy of right eye and temporal hemianopsia of left; undergrowth, sexual infantilism (Lorain type) delayed ossification, hypotrichosis, enlargement of sella turcica and probable tumor of hypophysis.

Case II. Female, age 9: Pre-adolescent pituitary insufficiency (dyspituitarism), Froehlich type, probably secondary to cerebral tumor; mental deficiency; nystagmus; optic atrophy; adiposity; sexual precocity; progressing paralysis and mental retardation.

Case III. Male, age 18: Pre-adolescent dyspituitarism, acromegalic stigmata; no sexual changes.

Case IV. Acromegaly in adult, with enlargement of sella turcica.—R. G. H.

(HYPOPHYSIS) Drugs to aid delivery. Benestad (G.) Norsk Magazin for Loegevidenskaben (Christiania), 1919, **80,** Suppl. 1-171.

Benestad discusses quinin and pituitary extracts, with ten pages of bibliography, giving the details of 111 cases in which one or more of these drugs were applied. The maximal dose of pituitary extract, he reiterates, must never be higher than twice the ordinary therapeutic dose. As a rule, one injection during the dilating phase and one during the phase of expulsion are all that should be used. The therapeutic dose of pituitary extract should correspond to not more than 0.10 gm. of the gland substance. In 71 per cent of his cases delivery proceeded spontaneously after a single injection of the pituitary extract. The failures were due to causes which the drug could not influence, extra large size of the fetus, rigid parts, etc. He advises operative delivery if the birth does not progress during the hour following the injection in the second stage of labor when the labor contractions are growing weaker. The effect seemed the same in primiparas and multiparas. J. Am. M. Assn., **72,** 1116.

(HYPOPHYSIS) DYSTROPHY adiposa genitalis in women, A study of—. Schumann (E. A.) Am. J. Obst. (N. Y.), 1918, **78,** 428. Abst. Surg. Gyn. and Obst., **28,** 150.

The syndrome resulting from the effects of deficient pitui-

tary secretion upon the female sexual system may be properly divided into three clinical groups, according to the sex epoch affected. Such terms as amenorrhea of obesity, and lactation atrophy or super-involution of the uterus are no longer correct, since it seems reasonably well proven that both conditions are but phases of a primary hypopituitarism. Definite retrogression of the reproductive tract may follow deficient pituitary secretion in parous women of mature age and may and frequently does give rise to erroneous diagnosis of pregnancy. Treatment for all groups consists in general measures and the empirical use of glandular extracts, the systolic blood pressure being a fair index of the particular gland substances to be employed—low pressure indicating pituitary and high pressure, thyroid.

The prognosis as to recovery is guarded in all cases, but is favorable in direct ratio to the age of the patient. (Quoted.)

(HYPOPHYSIS) Dystrophie genito-glandulaire. de Souza (O.) et de Castro (A.) Nouv. Icon. de la Salpét. (Paris) 1916-1917, **28,** 1.

This article is a presentation of illustrations and clinical history of dystrophia adiposo-genitalis as observed in Brazil.

—A. L. T.

(HYPOPHYSIS) Early pituitary syndromes. Pincherle (M.) Riv. di Clin. Pediat., 1918, **16,** 281, 337. Abstr. Brit. Jour. Child. Dis., 1919, **16,** 62.

The author gives full details of four cases and extensive tabulated results of experimental pituitary lesions, of the action of pituitary extract and clinical symptoms. He says that there exist morbid entities having the clinical course of diabetes insipidus, in which other symptoms indicative of disturbed pituitary function are found associated with polyuria and polydipsia. The most important of these are somatic under-development, excessive tolerance of carbohydrates, Cushing's thermoreaction, arterial hypotension, deficient secretion of sweat, asthenia and somnolence. In some of the author's cases the size of the sella turcica was markedly reduced and there were certain nervous phenomena indicative of participation of other endocrine glands. Moreover, he was able in some instances to produce a more or less marked, but always transitory, albuminuria by repeated forced lumbar lordosis. Pituitary organotherapy, although capable of reducing the polyuria and polydipsia, was powerless to effect a lasting cure.—M. B. G.

HYPOPHYSIS extract, Effect of—on nephritic processes (Wirkung von Hypophysenextrakt auf nephritische Prozesse). Glaessner (K.) Wiener med. Wchnschr., 1917, **30,** 1197-9.

Pituglandol usually acts as a diuretic in nephritis as in health; it also frequently (4 out of 6 cases) lessens the albumin and formed elements and causes blood, if present, to disappear. Whether this is simply due to diuresis or to a specific action on the kidney cells is not yet clear. Physiol. Abst., **3,** 331.

(HYPOPHYSIS) Familiäre akromegalieähnliche Erkrankung. Oehme (C.) Deutsche Med. Wchnschr. (Berl.), 1919, **45,** 207.

Description of acromegaly in 5 brothers and one sister.
—J. K.

(HYPOPHYSIS) Growth of normal and hypophysectomized tadpoles as influenced by endocrine diets. Smith (P. E.) Univ. California Pub. Physiology (1918), **5,** 11-22.

When the glandular lobe of the hypophysis was fed to normal tadpoles late in their larval cycle, a relative acceleration in growth occurred as the result of the retention of the 2nd growth cycle (period of rapid growth) beyond the normal point. During this late period all other larvae showed an extended period of retardation in growth (a prolonged 3rd growth cycle). When anterior lobe of the hypophysis was fed during this late period, the tadpoles reached a size somewhat above normal. Hypophysectomized tadpoles were retarded in growth on all diets except the glandular lobe of the hypophysis; the retardation was slight prior to the mid-larval period, but became very pronounced thereafter. While the rate of growth was retarded, the growth span was extended since metamorphosis failed to occur, and the hypophysectomized larvae thereby attained a size equal to or in excess of that of normal larvae. The retardation of growth in hypophysectomized tadpoles was entirely prevented by a diet of anterior lobe; a brief initial period was followed by a constant and accelerated rate of growth, so that these tadpoles exceeded in size (1) normal tadpoles on a control diet and (2) controls fed glandular lobe; they attained the maximum size far more rapidly, and exceeded in maximum size the hypophysectomized controls. Chem. Abst., **12,** 2385.

(HYPOPHYSIS) Hydroxybenzene radical in the acceleration of the growth of carcinomata by cholesterol and by tethelin. Robertson (T. B.) and Burnett (T. C.) J. Cancer Res., 1918, **3,** 75-91.

Other hydroxybenzene derivatives such as M-cresol, benzyl alcohol, hexahydrophenol, borneol and inositol do not cause any decisive acceleration of tumor growth. The accelerative actions of cholesterol and tethelin are not due to their possession of a hydroxybenzen group, but the accelerative action of cholestrol is in some way rendered possible by its possessing a hydroxyl group. The hydroxyl group may act as an anchoring group, fixing the cholesterol to the tissue, or it may merely facilitate the distribution of cholesterol throughout the tissue fluids by rendering the cholesterol emulsifiable. (Chem. Abst.) Physiol. Abst., **3,** 464.

(HYPOPHYSIS) Infantile DWARFISM (Infantiler Zwergwuchs). Stursberg. Deut. med. Wchnschr. (Berl.), 1919, **45,** 112.

A boy of 16½ years had grown normally up to the age of 10 when development ceased. The sella turcica is flat, and the testes small, but there is no eunuchoidism or evidence of malfunction of the thymus. S. believes that the condition is due to disease of the anterior lobe of the hypophysis.—J. K.

(HYPOPHYSIS) Lactation in an acromegalic patient (Auftreten von Milksekretion bei einem an Akromegalie leidenden Patienten). Roth (O.), Berlin klin. Wchnschr., 1918, **55,** 305-7.

The patient, a man of 28, secreted milk in the course of the disease. Physiol. Abst., **3,** 320.

(HYPOPHYSIS) Le rythme de la polyurie hypophysaire (Rhythm of hypophyseal polyuria). Bergé (A.) and Shulmann (E.) Presse Méd. (Paris) 1918, ..., 618-20.

An interesting history of a case of diabetes insipidus, together with a review of some of the older literature, mostly Continental. The quantity of urine excreted by this patient was variable, from 2000 to 5000 c.c. daily; the quantity of urine per hour was greater at night. At times excretion surpassed absorption of fluid, leading to a degree of dehydrating of the body. The chemical composition of the urine presented nothing noteworthy. There was no tendency to glycosuria. Functional tests showed that the kidney was normal. Posterior lobe pituitary extract produced a marked diminution in the urine formation and had a surprising tendency to relieve insomnia. At autopsy the anterior lobe of the pituitary was found invaded by gummata, while the posterior lobe was sclerotic.—R. G. H.

(HYPOPHYSIS) Lesion traumatique pure de l'hypophyse. Syndrome adiposo-genital et diabete insipide (Traumatic lesions of the hypophysis. Syndrome of dystrophia adiposo-genitalis and diabetes insipidus). Marañón (G.) et Pintos (G.) Nouv. Icon. de la Salpet. (Paris), 1916, **28**, 185.

The authors present in detail the clinical history and subsequent autopsy of a boy of 13 years, who had been accidentally shot in the head. The rifle ball lodged in the region of the stalk of the hypophysis. After a few months there appeared a development of secondary sexual features of the feminine type, together with excessive thirst and polyuria. Injections of extracts of the middle and posterior lobes of hypophysis very quickly caused temporary reduction of both thirst and diuresis. At autopsy, there was found a connective tissue overgrowth almost but not quite cutting off all nervous connections between the glandular portion of the hypophysis and the brain.

The authors also describe two other cases of diabetes insipidus, but without symptoms of dystrophia adiposo-genitalis. In both these instances pituitary extracts reduced the volume of urine and correspondingly increased the concentration of solids.

The authors maintain that diabetes insipidus consequent to hypophyseal injury is due essentially to hypopituitarism which, in turn, is relieved, temporarily, by pituitrin injections, just as definitely and specifically as myxedema is relieved by thyroid extracts.—A. L. T.

(HYPOPHYSIS) Pathological report on a case of pituitary infantilism. Evans (J. J.) and Assinder (E. W.) Birmingham Med. Rev., 1916, **80**, 1-6.

A man of 52 had stopped growing at the age of 12 or 14. He had worked comfortably as a lapidary until about 40, when failing vision and headaches developed. Later there were visual hallucinations which were augmented by attempts to relieve the symptoms by X-ray treatment. Thyroid and pituitary medication were of little or no benefit. Death occurred at 52. An autopsy showed a tumor in the pituitary fossa about the size of a hen's egg; this was identified as angioma. The ordinary stigmata of infantilism were present, as absent facial and pubic hirsutes, small genitalia, etc. The thyroid appeared under the microscope as hyperplastic, a finding interpreted by the author as indicating a relationship between the thyroid and pituitary glands.—R. G. H.

(HYPOPHYSIS) Pituitary headaches and their cure. Pardee (I. H.) Arch. Int. Med. (Chgo.), 1919, **23,** 174.

From a review of the literature and a consideration of seven cases, the author concludes that pituitary disturbances constitute a fairly common cause of headache. This headache is located between the temples, deep in behind the eyes, and is accompanied by dyspituitary signs. The sella turcica in most cases shows demonstrable abnormalities. In a large percentage of the cases these headaches and the accompanying symptoms disappear upon the administration of whole pituitary gland substance in doses varying from ¼ to 2 grains three times a day. Cases of progressive neoplastic growths were not benefitted by this treatment.—H. W.

(HYPOPHYSIS) Pituitrin in de verloskundige klinick. Knappert (J.) Nederlandsch Haandschrift voor Verloskunde (Leiden) 1916, **5,** 119-141.

A technical discussion of the indications for the use of pituitrin in obstetrics.—J. K.

(HYPOPHYSIS) Pituitrin in labor (—inspuitingen bij baring). de Monchy (M. M.) Nederl. Tijdschr. v. Geneesk. (Amsterdam), 1916, **60** (ii), 5-17.

Reports satisfactory results.—J. K.

HYPOPHYSIS, Pure traumatic lesion of the—(Lesión traumática pura de la hipófisis, síndrome adiposo-genital y diabetes insípida). Marañón y Posadillo (G.), Madrid, 1918, pp. 16.

A well illustrated exposition of the subject matter abstracted in Endocrin. 1919, **3,** 70.—R. G. H.

(HYPOPHYSIS) Un cas de dystrophie hypophysaire. Obregia (A.), Urechia (C.) et Popea (A.) Nouv. Icon. de la Salpet. (Paris) 1914-1915, **27,** 317.

The authors describe in detail the case history of a woman of 27 years with some of the symptoms of dystrophia adiposogenitalis, such as enlargement of the sella turcica, great excess of fat deposit, genu valgum, flat foot, moderate increase in urine output, frequent occurrence of epileptic attacks, incontinence of urine and low mental capacity. Menstruation was normal without any evident abnormality in sexual develop-

ment. They class their case as a "forme fruste de la dystrophie adiposo-genitale." In summary, they conclude this to be a rather typical instance of dystrophy from hypopituitarism.
—A. L. T.

HYPOPHYSIS, The anatomy of the—(Over een weinig bekend gedeelte der hypophyse). Woerdeman (M. W.) Nederl. Tijdschr. v. Geneesk. (Amsterdam) 1918, **62** (i), 215-21.

An accessory structure the "lobus bifurcatus" is described as developing embryologically in connection with the anterior lobe of the hypophysis. Later the connection is lost and it lies independent in the sub-arachnoid space. It is of some surgical interest since it occasionally gives rise to cysts. See also Endocrin. 1918, **2**, 174.—J. K.

(HYPOPHYSIS) Tumor of the pituitary gland; technique of operative approach. McArthur (L. L.) Surg. Clin. Chicago, 1918, **2**, 691.

Of technical surgical interest.

(HYPOPHYSIS, ADRENAL) The effect of some food hormones and glandular products on the rate of growth of paramecium caudatum. Chambers (M. H.) Biol. Bull. (Woods Hole), 1919, **36**, 82-92.

The author found that small amounts of pituitary extract added to hay infusion used as a diet for paramecia, caused an increase in their rate of division, but had the opposite effect when added to milk. Suprarenal extract caused an increase in the division rate of these protozoa when mixed with their diet of either hay infusion or milk. Shumway has reported an increase in the rate of division of paramecia when thyroid substance was added to their diet.—E. R. H.

INFANTILISM. Valdizan (H.) Revisto de Psyquiatria (Lima, Peru), 1918, **1**, 25-36.

Valdizan's five cases confirm the share of the endocrine system in the morbid tendency which is manifested by infantilism. All were young men, except one man of 56. In most of them the phase of infantilism followed some severe sickness, and under tonics and organotherapy clinically normal conditions were restored in time. Two were brothers, and albuminuria was among the first symptoms. He accepts it as an indication of the onset of the pluriglandular disorder, initiated in the

kidneys and spleen. This assumption is confirmed by the retrogression of this infantilism under a course of tonics. J. Am. M. Assn., **72,** 905.

(INTERNAL SECRETION) Over interne secretie. Vermeulen (H. A.) Tijdschr. v. Diergeneesk. (Utrecht), 1917, **44,** 155-64.

No new data presented.—J. K.

INTERNAL SECRETION, The so-called glands of—(Over zoogenaamde klieren met inwendige afscheiding). Lamers (A. J. H.) Nosokomos (Amsterdam), 1916, **14,** 224, 236, 280.

Three popular lectures on the internal secretions.—J. K.

INTERNAL SECRETIONS and enzymes, their inter-relation and inter-dependence, their value and application in modern therapy. McNulty (J. J.) J. Am. Inst. Homeopathy (N. Y.) 1918, **11,** 531-40.

A review, with special stress on the therapeutic value of polyglandular therapy. Chem. Abst., **13,** 47.

(INTERNAL SECRETIONS) Infantilism from ankylostomiasis. de Andrade (A. D.) Ann. Paul. de med. e chir., 1916, **7,** 133. Abstr. Brit. J. Child. Dis., 1919, **16,** 58.

The author reports six cases of infantilism in children, aged from 8 to 16 years, in which the condition was due to a pluriglandular syndrome caused by ankylostomiasis.—M. B. G.

INTERNAL SECRETIONS, Shell shock and the—: with suggestions as to treatment. Harrower (H. R.) The Prescriber (Edinburgh), 1916, **10,** 203-9.

Recent literature, largely French, indicating that the endocrine glands play an important part in shell shock is reviewed. It is suggested that opotherapy would be correspondingly valuable.—R. G. H.

INTERNAL SECRETION, The influence of—on the formation of bile. Downs (A. W.) and Eddy (N. B.) Am. J. Physiol. (Balt.), 1919, **48,** 192-98.

The authors show that the intravenous injection of secretin causes an increase in the amount of bile secreted, while adrenin, mammary, orchic, ovarian, pancreatic and thymic gland substances cause a decrease. The amount of bile secreted is

not affected in a constant or definite manner by the substances of the spleen and thyroid gland.—L. G. K.

(LACTATION) Acetonuria hos nôtkreatur. Eklund (J.) and Engfeldt (N. O.) Svensk. Veterinärtidskrift, 1918, **223,** 47.

A study of the acetonuria which appears in the cow in certain diseases in connection with lactation. Physiol. Abst., **3,** 452.

LACTATION in a calf. Fink (J. W.) Veterin. J. (Lond.), 1916, **72,** 28.

A description of a Holstein calf which began lactating at the age of a week and had continued to the time of writing, when a quart a day was being produced. Physiol. Abst., **1,** 239.

(MENSTRUATION) Date of fecundation. Razetti (L.) Gaceta Med. de Caracas, 1918, **25,** 232.

Razetti discusses the various theories in vogue and rejects all except those which accept the menstrual function as a preparation of the uterus for the embedding of the ovum. The internal secretion of the corpus luteum is what starts this preparation. According to this theory, there is no ripe follicle in the ovary during menstruation, and hence fecundation during this period is impossible. J. Am. M. Assn., **72,** 689.

MYASTHENIA gravis, with report of a case. Rosenheck (C.) J. Am. M. Assn. (Chgo.), 1919, **72,** 1211-12.

Includes no data of direct endocrine interest.—R. G. H.

(ORGANOTHERAPY) Concepto moderno de la opoterapia. Pita (A.) Medicina Moderna (Havana), 1918, **1,** 15-22.

A general theoretical discussion of the principles of opotherapy.—R. G. H.

ORGANOTHERAPY in relation to the practice of medicine. Starkey (F. R.) Northwest Med. (Seattle), 1916, **15,** 16-19.

A summary, perhaps too enthusiastic, of the use of organ extracts in the treatment of all sorts of diseases from myxedema to eclampsia and asthenopia.—J. P. S.

ORGANOTHERAPY, Rational—. Ghedini (G.) Gaz. d. Ospedali e d. Clin. (Milan), 1918, **28,** 9-12.

Ghedini insists that instead of using the extracts of organs we should use the venous blood issuing from the organ. This contains the true internal secretion, while the cells of the organ cease secreting this product when they are dead. Hence the removal of the organ from the body to make the extract not only arrests production of the internal secretion, but probably modifies essentially the delicate secretion already on hand in the tissues of the organ. Instead of a living secretion we get only a dead and possibly decomposed product. The efferent blood contains the secretion in its maximum vital potency. He published in 1911 research on the thyroid secretion thus obtained in the efferent blood, and in 1913 and 1915 similar research on the venous blood from the suprarenals, pancreas, and testicles. Manfredi announced in 1913 that the efferent blood from the pancreas inhibited certain actions of epinephrin. He cites further research since by Ollini, Masera, Durand and eight others. The difficulty of obtaining the efferent blood or lymph hampers and limits the research in this line, but this should be the goal toward which we strive. J. Am. M. Assn., **72,** 833.

OSTEOMALACIA. Selhorst (J. F.) Nederlandsh. Tijd. v. Geneesk. (Amsterdam), 1917, **2,** 2176.

In the case described the osteomalacia developed during a pregnancy and returned during the next pregnancy. Phosphorus was tried, but without success. Ovariotomy was followed by considerable improvement. Physiol. Abst., **3,** 228.

OVARIAN influences. West (G. R.) J. Tenn. State Med. Assn. (Nashville), 1918, **11,** 300-305.

A general discussion of the subject as related to practical medicine. No new evidence is adduced.—R. G. H.

OVARIES, Transplantation of—(Transplantation der Ovarien). Unterberger. Arch. f. Gynäk. (Berlin), 1918, **116,** 173.

Homoioplastic grafts, although they sometimes give temporary amelioration of symptoms are soon resorbed. Accordingly, injections or oral administration of ovarian material is ordinarily preferable. In cases of atrophy of the ovaries, however, such transplants at times give brilliant results. (The atrophic ovaries should not be removed.) Heteroplastic transplantation is possible only with the ovaries of monkeys. Autoplastic transplantation is nearly always successful. Small slices of the organ should be utilized, implanted, preferably, in the rectus abdominis. The two indications for this procedure

are benign tumors of both ovaries and purulent inflammation of both.—J. K.

OVARY, Cyclic changes in the interstitial cells of the, in the woodchuck (Marmota monax). Rasmussen (A. T.) Anat. Rec. (Phila.), 1918, **14,** 48.

See Endocrin. 1918, **2,** 353-404.

(OVARY) Hydatiform mole with ovarian cyst. Nordentoft (J.) Ugeskrift for Laeger (Copenhagen), 1918, **80,** 2139-43.

In Nordentoft's case the woman of 35 had borne three children. There was an interval of three years since the last pregnancy, but recently there had been no menstruation and a tendency to nausea and vomiting had convinced the woman that she was three months' pregnant. Then came severe hemorrhage by the vagina and the uterus seemed to be of a size corresponding to a six months' pregnancy. A large mole was found and the uterus curetted. A tumor rapidly developed thereafter on each ovary. On the left ovary the cystic tumor was 15 cm. long, with a base 8 cm. broad; on the right ovary the tumor was smaller, but both were of cystic structure, filled with a fluid, gelatinous mass similar to the contents of the mole. The uterus itself also showed suspicious patches so that supravaginal amputation seemed advisable. The patient has been in good health during the months since to date. The ovarian tumors had probably existed at the time of the operation on the mole, but their rapid growth, that could be followed with the eye and palpation, within less than a week, was most striking. In six other cases of mole given operative treatment at the same hospital, the women were from 20 to 46 years old; four of the women had borne several children, one only one child, and one was pregnant for the first time. Four have borne healthy children since; one woman died several months later of a pulmonary lesion which may have been metastasis from the mole, and one succumbed to sepsis consecutive to the operation. J. Am. M. Assn., **72,** 838.

(OVARY) Notes on superfetation and deferred fertilization among mice. Sumner (F. B.) Biol. Bull. (Woods Hole), 1916, **30,** 271-85.

Ovulation may continue during pregnancy. Physiol. Abst., **1,** 253.

(OVARY) Studies on the ovary of the spermophile (Spermophilus citellus tridecemlineatus) with special reference to the corpus luteum. Drips (D. G.) Am. Jour. Anat. (Phila.), 1919, **25,** 117.

The cycle of changes occurring annually in the ovaries of the spermophile is presented with detailed histologic descriptions of the corpus luteum at each stage of its development. Specific stains are used to bring out the nuclear and protoplasmic characteristics of the luteal cells. Three phases are thus noted in the life cycle of the corpus luteum: First, a phase characterized by the presence of great numbers of red granules, undoubtedly secretion granules in the protoplasm of the luteal cells. This phase embraces practically all of the period of pregnancy. Second, the lipoid phase, so called because of the abundance of lipoid droplets in the protoplasm of the cells. This phase begins some time before parturition and lasts for about six weeks afterward, which is also about the time the normal involution of the uterus becomes complete. Third, the phase of regression. Certain experimental studies are reported, such as the effects of single and double ovariectomy on pregnant and non-pregnant animals. Single ovariectomy is negative in results. Double ovariectomy in non-pregnant animals causes a very gradual functional atrophy of the uterus. In pregnant animals this procedure causes abortion except when it is very late in pregnancy. From the results of the histologic and experimental studies it is concluded that the corpora lutea produce two internal secretions which preside over changes occurring in the uterus incident to pregnancy. The early secretion effects the normal implantation and development of the embryo and the late lipoid secretion helps to bring about the normal involution of the uterus. Author's Abst.

(OVARY) The effects of hysterectomy upon ovarian function. Richardson (E. H.) Surg. Gyn. & Obst. (Chgo.), 1919, **28,** 146-52.

Published in abstract elsewhere. See Endocrin., 1917, **2,** 181.

OVARY, The relation of the supplying—to the causation of sex. Murray (J. G.) Johns Hopk. Hosp. Bull. (Balt.), 1918, **29,** 275-81.

This paper is devoted partially to a criticism of the evidence submitted by Dawson in a recent book, "The Causation of Sex in Man," and partially to an analysis of the records of 17,500 deliveries in the Obstetrical Clinic of the Johns Hopkins Hospital as bearing on Dawson's theories. The theory that

male children are derived from the right ovary and female from the left was tested in the case of 74 pertinent available records. In case of 47 male babies the corpus luteum was found in the right ovary in 55 per cent and in the left in 45 per cent of the mothers. In case of 28 female infants the corpus luteum occurred in the right ovary in 47 per cent and in the left, in 57 per cent.

Dawson's "rule" that ovulation occurs from the ovaries alternately and that, having established which ovary was involved in any given pregnancy, the prognostication of the sex of the offspring in succeeding pregnancies is possible, was also found to hold true in only half the cases. It is concluded that the supplying ovary has no influence upon the sex of the child and that male and female children result in about equal numbers from the fertilization of ova from either ovary.—R. G. H.

(OVARY) Tubal and ovarian hemorrhage. Its etiological relation to pelvic hematocele and extra-uterine pregnancy. Bovée (J. W.) Surg. Gyn. & Obst. (Chgo.), 1919, **28,** 117-22.

Published in abstract elsewhere. See Endocrin. 1918, **2,** 185.

Over glandulae PARATHYROIDEA. Vermeulen (H. A.) Tijdsch. v. Diergeneesk. (Utrecht), 1917, **44,** 155.

Published elsewhere. See Endocrin., 1917, **1,** 333.—J. K.

(PANCREAS) Diastatic activity of the blood in cancer, syphilis, and diabetes. De Noird (H. H.) and Schreiner (B. F.) Arch. Int. Med. (Chgo.), 1919, **23,** 484.

The diastatic activity of the blood of the ordinary syphilitic varies within normal limits. In the simple diabetic the diastatic action is extremely high. On the other hand, those diabetics who are syphilitic have a low diastatic activity. Both types have varying degrees of hyperglycemia. Five syphilitic diabetics demonstrated extreme loss of carbohydrate tolerance. This condition was materially checked by the cure of the syphilis. If it is possible to have a low diastatic activity and diabetes, then the disease does not depend solely on glycogenolysis, but may be due to the failure of the tissues to hold or burn sugar. It appears incredible that the islands of Langerhans should secrete an activating agent for diastase that sometimes activates and sometimes inhibits, but this must be true if one accepts the idea that pancreatic and syphilitic diabetes have the same cause—insufficiency of the secretion of the

islands of Langerhans—for in one case the diastatic activitiy is high and in the other low. Hence, it is suggested that the islands of Langerhans secrete a substance inhibitory to the secretion of diastase and thus control its activity. If this is true, then the increased diastatic activity in pancreatic diabetes is due to destruction of the islands to such an extent that there is no inhibiting agent of diastase secreted, and the diastase in the blood is super-active. In syphilitic diabetes, cirrhosis is not confined to the islands of the pancreas, but involves all parenchymatous tissue. This encroaches on the secretory cells which, in turn, are stimulated to excessive secretion. The diastase is inhibited to a greater degree, with a resultant low diastatic activity. Increased diastatic activity never accompanies hypo- or normal glycemia, but it is not uncommon to find hyperglycemia associated with a low diastatic activity.

The conclusion is drawn that the hyperglycemia of diabetes is due to another cause than increased glycogenolysis alone, and that it probably is something affecting the permeability of cell membranes to sugar and inhibition of glycogenolysis so that all or a great part of the sugar remains in the blood to be excreted. Hence, the internal secretion of the pancreas is probably inhibitory to the action of diastase in the blood.—H. W.

(PANCREAS) Marche de la glycosurie chez le chien dans les premières heures qui suivent l'ablation totale du pancréas (Development of glycosuria in the dog during the first hours following the total ablation of the pancreas). Bierry (H.) C. R. Soc. de Biol. (Paris.), 1919, **82,** 305-307.

Glycosuria appeared within five hours after removal of the pancreas. During the first hour after the appearance of sugar in the urine, the amount of sugar rapidly increases until it reaches 5 to 10 per cent.—F. A. H.

(PANCREAS) Observations concerning the pathology of pancreatic ferments. Wago (H.) Arch. Int. Med. (Chgo.), 1919, **23,** 251.

Not of endocrine interest.

(PANCREAS) The blood supply of the areas of Langerhans, a comparative study from the pancreas of vertebrates (Preliminary paper). Flather (M. D.) Anat. Rec. (Phila.), 1919, **16,** 71.

A comparative study was made of the arrangement of cells

and blood-vessels in the islet areas of the alligator, opossum, horse, raccoon, badger, skunk, rabbit, and guinea pig. The author concludes that while the vascular areas are extremely varied even in the same individual, there are certain distinctive features—shape, size, sinusoidal network, etc.—which characterize the islets in the different species of vertebrates. The paper is based upon a rather limited number of data, but more are promised for a later communication.—E. R. H.

PARATHYROID tetany, Studies on—. Wilson (D. W.), Stearns (T.), Janney (J. H., Jr.) and Thurlow (Madge DeG.), Johns Hopk. Hosp. Rep. (Balt.), 1916, **18,** 12-20. (Abstract of previous papers.)

The tetany resulting from parathyroid extirpation can be relieved by administration of acids. After the operation alkalosis may develop and be neutralized by the acid products resulting from muscular activity incident to tetany; the acidosis is associated with relief of the tetany. Ca salts as well as acid lower the dissociation constant of oxyhemoglobin and the alveolar CO_2 pressure. With development of tetany the elimination of acids and ammonia increases. After acute or chronic tetany acidosis may occur.—R. G. H.

(PARATHYROID) Tetany, Treatment of post-operative—by homoioplastic transplantation (Dauerheilung einer lebenbedrohenden postoperativen Tetanie durch homioplastische Epithelkörpertransplantation). Börcher (E.) Zentralbl. f. Chirur. (Leipsig), 1919, **40,** 34.

The only rational treatment of post-operative tetany is homoioplastic transplantation. A single large parathyroid is adequate. The operations upon both donor and recipient can be carried out under local anesthesia. The best locus of the graft is in the left externis abdominis muscle out of the way of a possible appendicitis incision. The procedure does not always result in complete disappearance of symptoms; psychic irritability and a feeling of weariness at times remain.—J. K.

(PARATHYROID, THYMUS) Parathyroids and calcium metabolism. Uhlenhuth (E.) J. Gen. Physiol. (Balt.), 1919, **1,** 315-322.

Three series each of 6 or 7 larvae of the salamander Amblystoma opacum were fed on thymus gland. The first series was otherwise untreated and each individual developed tetanic con-

vulsions, which ceased as metamorphosis approached. After metamorphosis all the larvae were free from tetany, although the limbs and feet remained permanently twisted and contracted and the muscles were permanently paralyzed. The second series was kept in a solution of calcium lactate. Tetany was less marked than in series I, but the permanent effects (paralysis and deformity) were quite as marked. Moreover several weeks after metamorphosis tetanic convulsions appeared. Series III was kept in a solution of magnesium lactate. These larvae acted similarly to those in Series II, except that the tetany was still less marked during the larval period.

The author believes with Biedl that the tetany toxin acts on the central nervous system to cause tetany and permanently to injure it. The muscular contractions may be prevented by the action of Ca or Mg salts, but no substance has yet been found which will antagonize the tetany toxin and so prevent its action on the central nervous system. Accordingly the most important function of the parathyroids is to prevent the tetany toxin from coming into contact with the central nervous system, by neutralizing it.—L. G. K.

PARATHYROIDS and calcium metabolism. Uhlenhuth (E.) Proc. Soc. Exp. Biol. & Med. (N. Y.) 1918, **16**, 20-21.

Larvae of a species of salamanders which have no parathyroid glands are thrown into tetany by the ingestion of thymus gland. It is supposed that this is due to a thymus toxin which is normally neutralized by the parathyroids. The more likely possibility that the tetany is due merely to improper diet is not discussed. Magnesium and calcium salts suppress to some extent the tetany, but can not prevent permanent lesions of the nervous system which result from thymus diet. These lesions result in permanent muscular spasms and paralysis.—R. G. H.

(PARATHYROIDS, THYMUS) The influence of milk upon tetany in Salamander larvae. Uhlenhuth (E.) Ibid., 1919, **16**, 51.

Milk has an effect similar to Ca and Mg.—R. G. H.

PARATHYROIDS, Contribution to the normal and pathological anatomy of the—(Contribución a la anatomia normal y patholόgica de las glándulas paratiroideas). Strada (F.) Actas del 1er Congress Nac. de Med. (Bs. Aires), 1916, **4**, 215.

See Endocrin. 1918, **2**, 516.

(PARATHYROIDS) CO_2 combining power of blood plasma in experimental tetany. McCann (W. S.) J. Biol. Chem., 1918, **35**, 553-63.

After parathyroidectomy in dogs, this rises coincident with the development of tetany. Both these phenomena also follow gastric operations which exclude acid from the duodenum. Tetany is considered to be an alkalosis in which a disproportion between the rates of secretion of acids and alkalis in the digestive tract may be a factor. No reference is made to the views of Paton and his colleagues.) Physiol. Abst., **3**, 453.

(PARATHYROIDS) Further studies of the influence of parathyroidectomy on the gastro-intestinal mucosa of dogs and rabbits. Friedman (G. A.) Jour. Med. Research (Boston), 1918, **38**, 69.

Thyroid insufficiency causes in dogs and rabbits acute ulcers of the stomach and duodenum which do not show a tendency to heal, due probably to permanent constitutional anomalies. Occasionally appendicular lesions are produced. In man minor degrees of thyroid insufficiency may cause the appearance of the initial lesion of peptic ulcer or appendicitis; but since the insufficiency is probably slighter than in thyroidectomized animals compensation may occur. Chronicity of the ulcer is due to other factors such as the constant irritation by food and an excessive amount of hydrochloric acid. The primary lesion is probably not due to infection, but to thyroid insufficiency. It is only after the initial lesion has been formed that invasion of bacteria and stagnation of feces help to develop the various forms of appendicitis. Diminished thyroid secretion in man may be responsible for the association of peptic ulcer and appendicitis, in the causation of the primary lesion of which the adrenals and parathyroids probably co-operate. The probable relation between them must be a functional one. The assumption of a disturbance in the endocrinous glands explains possibly the subtonic and hypertonic types of stomachs or peptic ulcer.—J. P. S.

(PINEAL?) Sexual precocity (Über vorzeitige Geschlechtsentwicklung. Obermann (W.) Deutsche med. Wchnschr. (Berlin), 1916, **42**, 196-98.

A boy of 4 is described. At birth he was normal. Soon he developed excessive hunger and was put on a diet of biscuits and cow's milk. At the age of one year there was hair on the genitals. At two years the genital development was that

of 18 years and the voice was deep. At 4 years acne appeared on the face and back, but there was no axillary or facial hirsutes. His physical strength and intelligence were excellent. The author discusses the possibility of disease of the pineal gland, but offers no specific evidence. No brain tumor was apparent.—J. K.

(PLACENTA) Secrezione interna della placenta e sua azione supra altre ghandole endocrine (Internal secretion of the placenta and its action on other endocrine glands). Ercole (C.) Ann. di Ostet. e Gin. (Milan), 1915, **37,** 225.

Injections of alcoholic extracts of placenta into guinea pigs and rabbits gave rise to manifestations of hypertrophy of mammary glands, uterus and vagina similar to that of normal pregnancy.

The adrenal cortex increased in size and cells of the thyroid gland simulated the appearance commonly assumed to represent an active state. The author considers that the corpus luteum of pregnancy differs from the corpus luteum of menstruation owing to the hormonic influence of the placenta. It is suggested that extracts of placenta may find clinical application in conditions of hypoplasia of the uterus; also in hemorrhagic metritis, and in changing ovarian activity towards the gravid type, favoring amenorrhoea.—A. L. T.

SECRETIN, Is vitamine identical with—? Jansen (B. C. P.) Geneesk. Tijdschr. voor Ned. Indié (Amsterdam), **58,** 191-7; Chem. Weekblad (Amsterdam), 1918, **15,** 1520-1.

Various statements occur in the literature about the identity of secretin with vitamine. Experiments showed that the vitamine from rice hulls is not identical with secretin. If it were, the fact could be used as the basis for a quantitative method of determining vitamine. An incidental result of the experiments was the observation that K salts injected into the blood vessels are poisonous! Chem. Abst., **13,** 466.

(SECRETIN) Chemical stimulation of the intestinal glands. Tomaszewski (Z.) Pflüger's Archiv. **170**, 260-312; Physiol. Abstracts **3,** 252-3.

Experiments were carried out on dogs with gastric and duodenal fistulas. Psychic influences were excluded as far as possible. Aq. or HCl extracts of stomach, various parts of small and large intestine, and pancreas were made and injected

intravenously or subcutaneously. Very little effect was obtained by intravenous injections, but after subcutaneous injection a flow of juice began in about 15 minutes and lasted 1-2 hours, as much as 350 c.c. of juice being collected in that time. In some cases the vagi were cut or atropine given, but the result was the same. The volume of juice obtained was proportional to the solid content of the extract used. Edkin's experiments were repeated, but in those cases where secretion of juice was observed, T. explains it as due to squeezing out of juice as the result of muscular contractions of the stomach wall. In any case the effect of pyloric extract was no more marked than that of an extract of fundus. The substance responsible for the secretion is an organic compound, stable at 100°, slowly decomposed at 130°, or by the action of pepsin, but not of trypsin. It is not identical with vasodilatin, since Witte peptone does not cause the secretion. The activity of the extracts is increased by treatment with 80% alcohol, but is slowly destroyed by absolute alcohol, ethyl or methyl. It is not extracted by Et_2O, $CHCl_3$ and is not precipitated by colloidal Fe or $HgCl_2$, but ¾ of the activity is lost by precipitation of the extract with phosphotungstic acid. Chem. Abst., **13,** 36.

(SECRETIN) Note sur la répartition de la sécrétine dans le duodénum et dans le jéjunum (Note on the distribution of secretin in the duodenum and in the jejunum). Métivet (G.) C. R. Soc. de Biol. (Paris), 1919, **82,** 274-275.

Confirmation of the work of Bayliss and Starling, showing that there is as much secretin in the jejunum as in the duodenum.—F. A. H.

(SEX) Contribution à l'histoire des femelles d'oiseaux chez qui se développent les attributs extérieurs du sexe male (Contribution to the history of female birds in which secondary male sex characteristics have developed). Larcher (O.) Rec. de Méd. Vét. (Paris), 1916, **92,** 173-83.

A valuable annotated bibliography of some sixty papers. —R. G. H.

(SEX) Féminisme post-ourlien (microrchidie et gynécomastie consécutives a une orchite double), presentation du malade (Feminism following double orchitis). Laignel-Lavastine and Courbon (P.) Bull. et Mém. Soc. Méd. d. Hôp. de Paris, 1917, **33,** 914-15.

A young man of 22, previously notably virile, had double orchitis following mumps. His virility disappeared and the external genitalia diminished in size, while the breasts developed marked hypertrophy. In general the patient approached the hermaphroditic type.—R. G. H.

SEX GLAND implantation, Further evidence on—. Lydston (G. F.) J. Am. M. Assn. (Chgo.), 1919, **72,** 396-98.

Progress of two cases earlier reported is discussed and four new cases are described. Continued favorable therapeutic results confirm the author's opinion that the procedure is of marked value in producing virility.—R. G. H.

(SEX) Several ways in which gynandromorphism in insects may arise. Morgan (T. H.) Anat. Rec. (Phila.), 1919, **15,** 357 (abstract).

Sex intergrades are very rare, 1:2200, in the fruit fly, Drosophila. They usually start as females. The author explains this gynandromorphism on the basis of loss of sex chromosomes. Nothing is said here of hormones.—E. R. H.

(SEX) The extent of the occurrence of sex intergrades in Cladocera. Banta (A. M.) Anat. Rec. (Phila.), 1919, **15,** 355-356 (abstract).

Sex intergrades in these small crustaceans are very rare, but when once established they tend to produce sex intergrades indefinitely.—E. R. H.

SPLEEN, The effect of the removal of the—upon the metabolism. Berlin (E.) Ztschr. f. Biol. (München), 1918, **68,** 371-90; J. Chem. Soc. 114, **I,** 360.

Extracts of spleen contain, besides choline, a substance which exerts a powerful action on the muscles of the uterus and intestine. The latter substance is not 6-amino-4-ethylglyoxaline. Both choline and the unknown substance occur also in a commercial extract of spleen, called "hormonal." Chem. Abst., **12,** 2355.

SPLEEN, The effect of the removal of the—upon the metabolism in dogs. Preliminary report. King (J. H.) Johns Hopk. Hosp. Rep. (Balt.), 1916, **18,** 7-9.

The idea that the spleen may have an obscure endocrine

function has not been entirely disproven. The observation that splenic extracts injected intravenously stimulate intestinal peristalsis is one that has been cited as indicating such a function. King made a careful metabolic study of dogs during a control period and after splenectomy. The metabolic processes were in general little affected, but an increase in the fats and cholestrin in the blood, together with increased absorption of fats and elimination of fatty acids were noted. The elimination of calcium was also increased.—R. G. H.

(SYMPATHETIC N. S.) MYASTHENIA, Studies with the plethysmograph and string galvanometer in—. Athanasiu (J.) and Marinesco (G.) C. r. Soc. Biol. (Paris) 1916, **79,** 545-548.

The authors conclude that the sympathetic, but not the cerebro-spinal system, is involved in myasthenia.—Physiol. Abst., **1,** 348.

(TESTES) Hypertrophy of the prostate. Mieremet (C. W. G.) Nederl. Tijdschr. v. Geneesk. (Amsterdam) 1918, (ii) 1474-81.

Mieremet presents a number of arguments to sustain the assumption that the hypertrophy of the prostate is due primarily to the action of a hormone from the testicles. If the hypertrophy were merely a tumor, then we might expect it to occur at any age, while in fact it affects almost exclusively men at a certain age. The phenomena observed with roentgen exposures of testicles and prostate also sustain his assumption. He thinks that not enough attention has been paid to the internal secretion of the testicles as a factor in enlargement of the prostate, and urges research on the testicles in cases of hypertrophied prostate.—J. Am. M. Assn., **72,** 386.

(TESTES) Influence of castration on the larynx of the large domesticated animals. Schreiber (J.) Anat. Anz., 1916, **49,** 129-150.

Experiments on horses and cattle show that castration of males in early life causes the larynx to remain in an infantile condition. Physiol. Abst., **1,** 249.

(TESTIS) Degeneration in the albino rat testis due to a diet deficient in the water-soluble vitamine, with a comparison of similar degeneration in rats differently treated and a consideration of the Sertoli tissue. Allen (E.) Anat. Rec. (Phila.), 1919, **16,** 93.

Albino rats fed by Osborne and Mendel on a diet deficient in the water-soluble vitamine were sterile. Examination of the testes showed complete degeneration of the germ cells. The Sertoli cells alone persisted in the tubules, though their nuclei were much shrunken. The interstitial tissue was hypertrophied. These conditions are the same as found in X-rayed testes of various mammals. Similar degeneration was found also in some rats alcoholized by MacDowell. It was present to a less degree in their non-alcoholized brothers. Under these conditions the Sertoli tissue reveals a syncytial structure which the author believes is the normal state, as shown by well-fixed material.

—Author's Abstract.

TESTIS, Transplantation of the—in man. Lichtenstern (R.) Münchner med. Wchnschr., 1916, **63,** 673-75.

After loss of both testes, transplantation of a testis from another man restores the previous physical and psychic condition. Experiments on animals are thus confirmed on man, and the hormone theory supported. Physiol. Abst., **1,** 249.

THYMUS and carcinoma, The connection between—(über Beziehungen zwischen Thymus und Karzinom). Kaminer (G.) and Morgenstern (O.), Wiener klin. Wchnschr., 1917, **30,** 41-5.

In animal experiments the addition of thymus to serum increases the power of the latter to destroy cancer cells. The administration of thymus lessens cancerous growths. Animals with persistent thymus are very insusceptible to cancer. The internal secretion of the thymus is thus believed to be a natural defence against carcinoma. Physiol. Abst., **3,** 330.

THYMUS and GONADS, The influence of feeding with—in tadpoles (Beeinflussung des Wachtums von Kaulquappen durch Verfütterung von Thymus und Geschlechtsorganen), Stettner (E.) Jahrbuch f. Kinderheilk (Berlin), 1916, **83,** 154.

A repetition of the experiments of Gudernatsch, who found that feeding thyroid hastened while thymus delayed metamorphosis. S. found that thymus feeding caused delayed metamorphosis, but not the excessive growth described by Gudernatsch. Inadequate bone formation frequently resulted in crooked tails; the tadpoles also showed abnormal configuration suggestive to the author of rickets in children. Feeding with testis or ovarian material caused slight delay of meta-

morphosis, but growth was normal and deformed tails not seen. Combined thymus and gonad exerted no apparent influence, a result due, possibly, to technical difficulties in adjusting dosages. Gudernatches results with thyroid were confirmed; the material produced very marked effects and minute doses only could be given without causing death.

See also Endocrin., 1917, **1**, 345.—J. K.

THYMUS, Influence of the—on the regeneration of bone (Beeinflussung der Regeneration von Knochenverletzungen durch die Thymusdrüse). Glaessner. Berl. klin. Wehnschr., 1918, **55**, 1127.

In the rabbit ingestion of thymus hastens the healing of fractured bone. Extension of the experiment to other animals and to man is advised to determine the practical significance of the results.—J. K.

THYMUS gland injection, The effect of—on the growth and behavior of the guinea-pig. An experimental investigation. Olkon (D. M.) Arch. Int. Med. (Chgo.), 1918, **22**, 815.

Intraperitoneal injections of thymus preparations often resulted in muscle spasms, dyspnea and convulsions. These spasms appeared more severe and of longer duration than those following the injection of muscle or one-tenth normal sodium chloride solutions. Emaciation, accompanied by dryness and roughness of the fur, and loss of weight followed the continued use of thymus preparations.—H. W.

(THYMUS) Nature of the retarding influence of the thymus upon amphibian metamorphosis. Uhlenhuth (E.) J. Gen. Physiol. (Balt.), 1919, **1**, 305-313.

The author found that, although thymus-fed salamander larvae often metamorphose normally, thymus feeding sometimes retards and in rare cases completely inhibits metamorphosis. This action, however, is very inconstant and variable, completely unlike the constant effects of the tetany producing substance of the thymus and the metamorphosis producing substance of the thyroid.

When normal food is added to the thymus diet the inhibitory effect does not appear. Also the addition of a small quantity of Bayer's iodothyrin rapidly leads to precocious metamorphosis of thymus-fed larvae. The conclusion is therefore reached that the inhibitory effect of the thymus is not due

to a specific inhibiting substance, but to the absence from the diet of the thymus-fed larvae of a substance required to develop the thyroid to the secretory state. Such a substance might occur in the connective tissue of the thymus, and since some of the larvae no doubt obtained more of this tissue than others, the great variability of the results could thus be explained.

—L. G. K.

(THYMUS) Thymectomy after failure of radiotherapy (Un cas de thymectomie sous-capsulaire pour hypertrophie du thymus, apres échec de la radiothérapie). Chaton. Rev. internat. de Méd et de Chis. (Paris), 1917, **28,** 105-6.

Of technical surgical interest. The radio-therapy had apparently left the thymus tissue normal.—R. G. H.

(THYMUS). Über die Funktionen der Thymusdrüse vom Standpunkte ihrer Ausfallserscheinungen (The function of the thymus considered from the effects of extirpation.) Tangu (Y.), Mitt a. d. Medizin. Fakultät. Tokyo Univ., 1916-17, **16,** 539-605.

The first series was extirpation, with autoplastic transplantation into the mesentery. The operation was performed on 40 dogs, of various breeds; of these seven lived (three controls); all of the others died from causes unavoidable, shock, disease, infection, etc. There was no difference in skeletal measurement, calcium content, or epiphysis. The conclusion is naturally drawn that either extirpation has no effects or that the transplanted organ has functioned.

In order to determine the normal period of involution of the thymus an unusual number of observations was made on the absolute and relative weight of the gland in dogs of the same litters and then reduced to a standard. The author comes to the following conclusion: Involution does not begin until the fourth month (gross weight and microscopically). During the first—second week the ratio of thymus to body weight is the least, 1:189. This observation is important in considering the most opportune time to extirpate to obtain the most marked effects.

A great number of animals was used and exhaustive examinations made of fatal cases and of those that were ultimately killed. Both clinical and biological tests were employed.

The results may be tabulated as follows, no observations being included where a proper control was lacking:

I. Body weight—no change after thymus extirpation.

II. Growth—no three stages as reported by Klose and Vogt.

III. Nervous, Psychic, etc.—no effect.

IV. Blood corpuscles—no change in number or differential count.

V. Change in opsonic index—none. The alexin action of the blood serum is lowered for several weeks and then recovers, probably due to the activity of other alexin producing tissues, bone marrow, spleen, etc.

VI. Blood pressure—results conflicting.

VII. Histological—there were generally small patches of thymus cells in the body, due either to regeneration (?) or accessory thymus-granular structures.

VIII. Skeletal changes—no change in length, cellular structure, calcium content or callus formation after fracture of epiphysis.

IX. Change in other organs—no change macroscopic or microscopic in any of the other internal secretory organs, epithelial tissues or lymphoid tissues.

On the whole the evidence convincingly indicates that the thymus is not an organ of internal secretion.—W. E. B.

(THYROID) A discussion of goitres in 583 registrants. Levin (S.) J. Mich. State Med. Soc. (Grand Rapids), 1919, **18,** 98-104.

An interesting contribution to the statistics of endemic goitre. Levin, as examining surgeon, collected data on 583 registrants for military service. The locality from which the men came is in the "goitre belt" in the Great Lakes district. The proportion of the men born in the locality was 95 per cent. Of the 583, 177, or 30 per cent, showed demonstrable enlargement of the thyroid. Of these 140, or 24 per cent were classified as simple goitres; 3.9 per cent, toxic goitres and 2.4 per cent were large goitres of the adenomatous, colloid or cystic types. The incidence of goitre in the group studied decreased with age, possibly because more of the older men were born outside the district.—R. G. H.

(THYROID ADRENAL) The stimulation and inhibition of the gastric secretion which follows the subcutaneous administration of certain organ extracts. Rogers (J.), Rahe (J. M.), and Ablahadian (E.) Am. Jour. Physiol. (Balt.), 1919, **48,** 79-92.

Slightly alkaline extract of the non-coagulable material

from the thyroid gland was found to be a vigorous stimulant to gastric secretion, when injected into the subcutaneous tissue of the neck, in dogs. The effect produced was attributed, in part at least, to an intensification of the functions performed by the terminal filaments of the (gastric) vagus. Atropin checked, but did not prevent the increased gastric flow produced by the thyroid extract. Extracts similarly made from adenomatous or hypertrophied human glands were found to be inert. Extracts of the adrenal gland vigorously inhibit gastric secretion, supposedly by an intensification of the inhibitory function of the sympathetic. Adrenalin is not as active a gastric inhibitor as the adrenal nucleo-proteins obtained from extracts of the whole gland. These nucleo-proteins contain only traces of epinephrin. Extracts of the pituitary also inhibit gastric secretion, but only about one-half as vigorously as do extracts of the adrenal.—L. G. K.

(THYROID) A few facts in regard to modern X-ray therapy. Bellaire (R. F.) Minnesota Med. (St. Paul), 1918, **1**, 380.

Among several other conditions mentioned "hyperthyroidism" is mentioned as amenable to roentgen therapy. Clinical cures of toxic goitres are obtainable in 80 per cent of the cases. The chest in all instances should be rayed from both front and back to include the thymic area.—R. G. H.

(THYROID) A propos d'un syndrome basedowein d'origine émotive survenu chez un addisonien. Etude pathogénique. (Concerning the syndrome of Basedow's disease of emotional origin occurring in an individual suffering from Addison's disease.) Etienne (G.) et Richard (G.) Soc. Méd. des Hôp. de Paris, 1918, **42**, 1199.

As evidence against the theory that exophthalmic goitre has origin in hypersecretion of the adrenal glands, which in turn may possibly function as exerting a sympathicotonic influence over all endocrine organs, Etienne and Richard report a case of frank Addison's disease, in which psychic trauma caused the sudden appearance of symptoms of exophthalmic goitre. Here obviously there was a condition of adrenal deficiency, yet emotional causes appeared to be immediately responsible for an acute appearance of thyroid abnormality, presumably hyperactivity.

This does not prove the non-existence of a sympathetic origin of this type of goitre, but rather that the intermediation of the adrenal glands does not appear to be a necessary factor.

—A. L. T.

(THYROID) An unusual combination of cardiac arrhythmias of atrial origin occurring in a patient with focal infections and thyroid adenomata. Barker (L. F.) and Richardson (H. B.) Arch. Int. Med. (Chgo.), 1919, **23,** 158.

Report of a case in which marked disturbances of cardiac rhythm were encountered in association with peridental, maxillary and tonsillar infection and minute adenomata of the thyroid gland. Marked improvement followed treatment of the infected foci and partial thyroidectomy. Electrocardiographic studies of the case demonstrated at one time or another the following: (1) Physiological rhythm; (2) Dislocation of the pacemaker from the sino-atrial node to points elsewhere in the atrium; (3) Alternate atrial extra-systoles, none of which provoked a ventricular response; (4) Alternate atrial extra-systoles, many of which provoked a ventricular response; (5) Paroxysmal tachycardia; (6) Atrial flutter.—H. W.

(THYROID) A report on goitre among draft men from the Northwest. Brendel (F. P.) and Helm (H. M.) Arch. Int. Med. (Chgo.), 1919, **23,** 61.

An examination of 8,951 drafted men showed that goitre is more common in young men from the Northwestern States than the experience of the general practitioner would suggest. Apparently there are definite goitre districts existing in Oregon, Montana and probably in Nevada. Locality seems to be of greater etiological importance than heredity. The more toxic cases, in addition to the classical cardiac symptoms, show a tendency to nephritis.—H. W.

THYROID carcinoma among the salmonoid fishes. McHenry (H. H.) Med. Review of Reviews (N. Y.), 1916, **22,** 732-36.

This is a study of the enlargements of the thyroid and the carcinoma found among the salmonoid fishes. The disease occurs rarely in wild fish, but very commonly in those kept in captivity. McHenry concluded that the geologic formation at the source of the water in which the fish were kept had nothing to do with the development of the disease. The disease occurred in ponds and troughs of all descriptions. The incidence of carcinoma increased with age. In the thyroid glands of some fish nematode worms were found. Scrapings from the inside of the troughs containing fish with thyroid carcinoma were fed to four dogs for six months. All of these developed marked thyroid hyperplasia, and one of them showed a grossly detectable enlarged thyroid. The author thinks that these

enlargements and changes are the first stages in mammals of the same thyroid disease which occurs among the fish. In the hyperplastic thyroids of three puppies and of one adult dog which were given infected water, minute nematode worms were found immediately beneath the capsule or in the substance of the gland. If these worms have any etiologic significance it is probably merely as carriers of the causative agent. McHenry thinks that man would acquire thyroid disease from drinking water occupied by infected fish.—J. P. S.

(THYROID) Cretinism. Lattimore (E. B.) Charlotte Med. J. 1917, **76,** 206.

Brief description of two cases which reacted favorably to thyroid medication.—R. G. H.

(THYROID) Cretinism, A case of complete—with normal mentality. Hoag (W. B.) N. York Med. J., 1916, **103,** 791.

Published elsewhere. See Endocrin., 1918, **2,** 337.

(THYROID) Diagnosis and treatment of non-toxic goitre. Scott (C. M.), West Va. Med. J. (Huntington), 1916, **11,** 169-70.

No new data.—R. G. H.

(THYROID) Een geval van struma van het paard. Hartog (H. J.) and Loran (G. J.) Tijdschr. v. Diergeneesk (Utrecht), 1919, **46,** 93.

Describes a case of goitre in a horse.—J. K.

(THYROID) EXOPHTHALMIC GOITRE in relation to ovarian insufficiency (Des relations de goitre exophthalmique avec l'insuffisance ovarienne). Tilmant (A.) Presse Méd. (Paris), 1919, —, 164.

A brief presentation of six cases in women of the same family in whom the appearance of the thyrogenic symptoms coincided with periods of ovarian disorder (as menopause). It appeared that the thyroid disorder was due to a transmitted hereditary tendency.—R. G. H.

(THYROID Exophthalmic goitre, nervous and mental symptoms in—. Barker (L. F.) Med. Press (Lond.), 1919, **107,** 85-87.

Reprinted from J. Am. M. Assn., 1918, **71**, 327-29. See Endocrin. 1918, **2**, 343.

(THYROID) Exophthalmic goitre, peculiarities in the symptomatology of—. Bram (I.) Med. Rec. (N. Y.), 1919, **95**, 358-60.

Bram believes that thyroid dysfunction is an important, unrecognized factor in many disorders. By the time the classical "tetrad" of "hyperthyroid" symptoms is clearly in evidence much harm to the individual may have been done. Even an enlarged thyroid may produce local manifestations, the cause of which is frequently overlooked, such as cyanosis, headache, vertigo, epistaxis, "vagotonic" (irritative) symptoms, dyspnea, dysphagia and dysphonia. The enlargement may be in an inward direction and thus escape detection. Obscure symptoms due to excess thyroid secretion are very numerous; among these are emotional instability, glycosuria, polyuria, loss of weight and noctural sweating suggestive of tuberculosis. The diagnosis of exophthalmic goitre is accordingly beset with pit-falls. In the presence of symptoms which cannot be brought into line otherwise, the thyroid gland should always be taken into account.—R. G. H.

(THYROID) Exophthalmic goitre, Successful therapy of—. Brown (I.) N. Y. Med. J., 1919, **109**, 314-21.

The relative virtues of surgical and non-surgical treatment are again debated with the author strongly favoring the latter. The successful treatment of three cases is given in detail. It is insisted that individualization of treatment is essential to success. The importance of maintaining good digestion is especially emphasized.—R. G. H.

(THYROID) Exophthalmic goitre, The aorta in—(L'aorte dans le goitre exophthalmique). Folley (C.) C. r. Sec. de Biol. (Paris), 1918, **166**, 830-31.

Further evidence of aortic dilatation (abdominal) in exophthalmic goitre. See Endocrin., 1918, **2**, 342. Physiol. Abst., **3**, 265.

(THYROID) El reflejo oculo-cardiaco en el hipertiroidismo (The oculo-cardiac reflex in Graves' disease). Marañón (G.) Boletin Soc. Española de Biol., 1916. Session, May 26.

It has been reported that pressure on the eye-ball produces

a greater slowing of the pulse in exophthalmic goitre of the "vagotonic" than of the "sympatheticotonic" type and that this phenomenon has diagnostic and prognostic value. Marañón tested the theory in 47 cases of all types of "hyperthyroidism" of various degrees of severity. Slowing of the pulse eight or more beats per minute was regarded as "positive," less than eight "negative" and acceleration of the pulse "inversion." In the 47 cases reported the reaction was positive in 61.7%, negative in 34% and inverted in 4.2%. No relation could be established between symptomatology or severity of the disease and the sign or character of the reflex. Marañón regards it, therefore, as useless either for diagnosis, prognosis or as determining treatment.—R. G. H.

(THYROID). Esperimenti di innesti eteroplastici di tiroide Basedowiani. (Heteroplastic transplantation of thyroid glands of exophthalmic goitre). Agata (G. D.) Lo Sperim. (Firenze), 1918, **71,** 392.

Small portions of human thyroid glands from true cases of Graves' disease were transplanted into rabbits and dogs. The grafts rapidly autolysed and became infiltrated by connective tissue from the surrounding tissue. The engrafted tissues degenerated equally in normal and in thyroidectomized animals.—A. L. T.

(THYROID) Experimental investigations of ENDEMIC GOITRE. Hirshfeld (L.) and Klinger (R.) Arch. f. Hygiene (München) 1916, **85,** 139-188.

As a result of the authors' study of the disease, combined with experiments on animals, the essential condition of the change is regarded as of metabolic origin; protein metabolism is specially affected, and the cause is probably specific, though not yet ascertained. The hypothesis that it is due to lack of iodine is rejected. Physiol. Abst., **1,** 245.

THYROID Gland, Acute necrosis of the—. Bevan (A. D.) Surg. Clin. Chicago, 1918, **2,** 1089. Abst. Surg. Gyn. & Obst. (Chgo.), **28,** 300.

An unusual case of subacute infection of the thyroid in a man of 60 is described. A hard, tender, deeply situated mass above the sternoclavicular articulation associated with systemic symptoms suggested septic thrombus of a large vein. Operation disclosed an inflamed thyroid which upon section showed

round cell infiltration but no pus. The wound was kept open and packed with iodoform gauze. Recovery did not take place and the diagnosis of thrombosis was repeated. Further operation showed a total necrosis of the right lobe of the thyroid, which was removed, leading to prompt recovery. Upon encountering a similar case in the future the author would immediately extirpate the affected lobe.—R. G. H.

THYROID gland, A proving of the—. Gillingham (H. P.) Homeopathic Recorder (Lancaster, Pa.), 1918, **33,** 481-89.

An interesting series of experiments on thyroid feeding in six young women and in four guinea pigs, reported in the technical terminology of the homeopathic sect. In all, over 900 "symptoms" were produced which, by elimination of those obviously not due to the drug and of repetitions, were reduced to 407. Many of these were subjective, and some due, apparently, to an intercurrent rhinitis. Menstruation was delayed in one and hastened in four cases, with increased pain in all but one. An extended report is promised.—R. G. H.

THYROID gland, Brief synopsis of the structural changes occurring in the—when diseased. Vass (T. E.) West Va. Med. J. (Huntington), 1916, **11,** 171-2.

No new data.

THYROID gland, Relation between—, metamorphosis and growth. Uhlenhuth (E.) J. Gen. Physiol. (Balt.), 1919, **1,** 473-82.

From studies on the growth curve and age of metamorphosis of Amblystoma opacum the author concluded that two substances are involved in amphibian metamorphosis; first, iodine, which is taken up from the food and stored by the thyroid gland, and second, an excretor substance, which is evolved during the processes of growth and induces the excretory function of the thyroid. This hypothesis explains why in larvae, whose metamorphosis is inhibited by lack of iodine (by a thymus diet), there is a drop in the growth curve at the time metamorphosis should occur; for at this time the excretor substance begins to act and this results, since iodine is absent, in the excretion by the thyroid of a toxic substance, (probably the amino-acid tryptophane which is normally used to build up the thyroid hormone), which causes the breakdown of proteins and consequently a decrease in size of the larvae. Larvae

whose metamorphosis is inhibited by extirpation of the thyroid or by the hereditary lack of a thyroid (as in the case of Typhlomolge) show no drop in the growth curve, since in them the action of the excretor substance cannot result in the excretion by the thyroid of a toxic growth-inhibiting substance. At low temperatures less excretor substance is produced than at high temperatures during an equal rate of growth; consequently larvae kept at a low temperature reach a larger size than larvae kept at a high temperature, before they metamorphose.

—L. G. K.

THYROID gland, Syphilis of the—. .Report of a case. Schneider (E. H.) Calif. State J. Med. (San Francisco), 1918, **16,** 484-85.

The patient, a woman of 48, gave a history indicating adenoma of the thyroid persisting 17 years. Upon the development of tertiary syphilis in the thyroid, the goitre disappeared. The luetic manifestation began as a slowly growing, painless induration involving the thyroid gland and the overlying muscle. The neighboring lymph glands were not enlarged. There appeared an area of caseation in the sternothyroid muscle, with general fibrosis of the thyroid and adjacent tissues. The diseased portion of the gland was removed and, upon the discovery of a positive Wasserman reaction, anti-luetic treatment was instituted, leading to complete restoration to health. The microscopic picture in the thyroid removed confirmed the diagnosis of syphilis. The theory that normal thyroid tissue will not harbor Treponema on account of the iodine present is mentioned.—R. G. H.

THYROID glands, van Os (D.) Pharm. Weekblad. (Amsterdam) 1918, **55,** 1426-31.

Unlike most pharmaceuticals, thyroid preparations are not standardized according to any adequate system. The usual plan of stating strength in terms of the weight of the fresh glands and gauging the dose accordingly, is very unreliable because of wide variations in the amount of fat and H_2O in the fresh glands. This is especially true of the glands from sheep. The I content of the dried, fat-free powder is fairly constant in preparations from sheep (ranging in 5 samples from 0.355 to 0.38%), but less so in those from swine (ranging in 7 samples from 0.15 to 0.266%). The Holland Pharmacopeia requirement of 0.4% should be lowered to not more than 0.3%. Experiments failed to show that I takes any part in the action of thyroid

preparations. Since neither a chemical nor a physiological method of standardization is practicable, the most reliable basis for expressing the strength and calculating the dose is the weight of the dried, fat-free powder.—Chem. Abst., **13,** 360.

(THYROID) Goitre, A summary of the surgical treatment of—. Porter (M. F.), Surg. Gyn. & Obst. (Chgo.), 1919, **28,** 431-2.

Generally speaking, surgical services are sought by goitre patients because of (1) toxic symptoms, (2) pressure symptoms, (3) deformity, and (4) a combination of these. Porter feels that it is highly important that patients with benign goitres be urged to have them treated, on account of the danger of their becoming toxic. In all patients who are good surgical risks subtotal thyroidectomy is the operation of choice. The general belief that the hyperactive portions of a hypertrophic thyroid are marked by redder color than the remainder of the gland is not borne out by Potter's observations. The trouble-producing portion, as indicated by microscopic determination, has at times been found lighter and softer than the remainder. Various details of surgical interest are included. Especial emphasis is laid on the importance of foci of infection in goitre patients. Removal of these will at times cause the disappearance of the goitre. To leave such foci after a goitre operation is to invite recrudescence of the goitre and expose an especially vulnerable patient to extension of the infection.—R. G. H.

(THYROID GOITRE) Notes on radium treatment. Turner (D.) Edinburgh Med. Rev., 1919, **22,** 79-86.

Turner has treated to date upwards of 50 cases of exophthalmic goitre with radium and, with one exception, all have been in some degree benefited. The one exception was a woman of 22, who died within two weeks after the treatment, of toxic thyroidism. The benefit that patients with exophthalmic goitre derive from the expert application of radium is in their general condition and in their general symptoms. They regain strength and weight and the tachycardia, tremor and breathlessness diminish or disappear. The thyroid gland becomes harder, but usually not smaller, a fact of which it is wise to forewarn the patient, to prevent disappointment. Exophthalmos is little affected. Cosmetic operative measures can later safely be taken if desired. Turner treats each lobe and the isthmus of the thyroid, and the thymus. A dose of 200-400 milligram hours, with proper screening, is given, over each area, and the patient sent home for three months. Then, if necessary, the treatment

may be repeated. The skin in the throat region is very sensitive to the rays and must be carefully protected. As compared with X-rays, radium permits more exact dosage, penetrates better and is not disturbing to a nervous patient.—R. G. H.

(THYROID) GOITRE, Pathology of—, based upon specimens received at the State Institute for the Study of Malignant Disease, Buffalo, New York. Simpson (B. T.), Surg. Gyn. & Obst. (Chgo.), 1919, **28,** 153-58.

Thyroid enlargements fall into the following groups:

Simple goitre
  Physiological
  Toxic
Multiple adenomata
  Cystic
  Solid
Colloid goitre
Exophthalmic goitre
Neoplasms

These differ markedly from each other and should receive correspondingly differentiated treatment. Multiple adenomata form the commonest type. They begin probably in remnants of embryonic ducts at about the age of puberty; later they tend to the degenerative changes which give this type its numerous names. When very cellular these adenomata may cause intoxication. Exophthalmic goitre is due to excessive secretion, whether normal or not. Five per cent of the specimens showed combinations of the foregoing types.—R. G. H.

(THYROID) Graves' disease, The treatment of—(Erfahrungen und Studien über die Basedowsche Krankheit und ihre operative Behandlung). Hilderbrand, Arch. f. klin. Chir. (Berlin), 1918, **111,** 1.

In most cases, according to Hilderbrand, surgical treatment, and in a few, even repeated operations, are indicated. In his experience 54 per cent were entirely cured and 34.3 per cent improved. Although in many cases a persistent thymus plays an important role, this often is not found. Very frequently symptoms are seen which can best be explained as due to "hyperadrenalinemia."—J. K.

(THYROID) Hyperthyroidism. Marshall (H. P.) Northwest Med. (Seattle), 1916, **15,** 8-11.

This is a brief, systematic discussion. The author emphasizes the observation that "most cases of hyperthyroidism belong to the constitutionally nervous class, and have at some time or other passed through either a severe psychic or a severe physical strain." He divides hyperthyroidism into two types: (1) low grade hyperthyroidism accompanied by non-hyperplastic goitre and in which parenchymatous degenerations predominate over toxic functional disturbances; and (2) high grade hyperthyroidism, usually accompanied by hyperplastic goitre in which toxic disturbances prevail. He thinks that all cases should be given medical treatment until it is evident that no improvement is to be expected. Then surgical interference is justified.—J. P. S.

(THYROID) Hyperthyroidism, Contribution to the study of—(Contributo allo studio dell' ipertiroidismo: le variazioni dell' acqua, dell' azoto e del glicogene nei principali tesuti degli animali ipertiroidati). Sega (A.), Bull di Sc. Med. di Bologna, 1916, **87,** 125-42.

A rat, two rabbits and two dogs were fed large quantities of thyroid gland. The tissues were desiccated and analyzed for nitrogen and glycogen. The results are reported at length. No conclusions of general interest were reached, except that hydremia results from such treatment. The paper is chiefly of technical interest.—R. G. H.

(THYROID) Hyperthyroidism, Several cases of—, including three of acute Graves' disease, in soldiers (Einige Fälle von Hyperthyroidismus, darunter drei von akutem Basedow bei Kriegsteilnehmern). Rothacker (A.) Münchner med. Wchnschr., 1916, **63,** 99.

Rothacker describes six cases of Graves' disease which developed after the psychic strain of participating in battle. They were perfectly cured by rest. The cases are regarded by the author as demonstrating that the thyroid condition is not the essential factor in the disease, but that the symptoms, of which hyperthyroidism is one, are purely of psychic origin.
—J. K.

(THYROID) Hypothyroidism, Brown (J. R.) Northwestern Med. (Seattle), 1916, **15,** 5-8.

The author states that the function of the thyroid is (1) to act as a stimulus to growth and development; and (2) to cause

the oxidation of the waste matter of cell degeneration into end products easily excreted by the lungs, skin and kidneys and (3) to influence menstruation, pregnancy and lactation. True myxedema is rare, but mild thyroid deficiency is very common, especially in the Puget Sound country, as shown by the large number of compensatory goitres one sees daily. A list is given of twelve objective symptoms suggestive of thyroid deficiency. Seven cases are briefly reported and the difficulty of determining the right dosage in thyroid medication is emphasized. When thyroid medication is followed by loss of weight, a correct diagnosis has been made. This loss of weight continues until the infiltrating mucin has been displaced, after which no further loss occurs no matter what dose is used. The author believes that the simple enlargement of the thyroid in children and young persons is probably always an expression of hypothyroidism and recommends the use of thyroid extract.

—J. P. S.

(THYROID HYPOPHYSIS) Effect of extirpation of the thyroid gland upon the pituitary gland in bufo. Larson (M. E.), Anat. Rec. (Phila.), 1919, **15**, 253-254 (abstract).

The anterior lobe and pars intermedia of the hypophysis both increased in size after removal of the thyroid. The nuclei of the hypophysis of the experimental larvae were more nearly spherical than normal and the gland itself was less compact. The gland normally decreases in size during metamorphosis.

—E. R. H.

(THYROID HYPOPHYSIS) Miscellaneous notes regarding experimental studies upon the endocrine glands of rana and bufo. Allen (B. M.), Anat. Rec. (Phila.), 1919, **15**, 353 (abstract).

Tadpoles from which removal of the thyroid had been attempted and which metamorphosed later than normal were found to have imperfect thyroids. Three animals from which removal of the hypophysis had been attempted gave the usual pigmentation reaction of larvae without hypophysis, but metamorphosed and were found to have imperfect hypophyses. Keeping hypophysisless tadpoles in dilute solutions of pituitrin did not stimulate pigment production. Hypophysis of cattle had no effect when fed to thyroidless tadpoles. The parathyroids (epithelioid bodies) of thyroidless larvae were larger than normal.—E. R. H.

(THYROID HYPOPHYSIS) Results of extirpation of both thyroid and pituitary glands in tadpoles of bufo and rana. Allen (B. M.), Anat. Rec. (Phila.), 1919, **15,** 252-253 (abstract).

The author found that removing both the thyroid and hypophysis fundament gave results similar to removing only the latter, in regard to retarded growth and development and deficiency of pigmentation. The limbs were retarded in growth in the same manner as after extirpation of either the thyroid or hypophysis. The germ glands developed proportionally with the size of the body.—E. R. H.

(THYROID) Infantiel myxoedeem. Scheltema (G.) Nederl. Tijdschr. v. Geneesk. (Haarlem), 1919, **63,** 637.

Treatment of infantile myxedema never results in complete normality; abnormal bone structure always persists.—J. K.

THYROID insufficiency, The frequency of—in general practice. Johnson (R.) Dub. Jour. Med. Sc., 1917, **144,** 297-309. Abstr. Brit. Jour. Child. Dis., 1919, **16,** 60.

In treating a case it is well to have the eyes tested, since the headaches complained of are often lessened by the use of correct glasses. It is noteworthy that glasses worn before the taking of thyroid gland often have to be altered after a month or more of regular doses. Experience is the only teacher in the administration of the correct dose of thyroid. Small doses should be given at first, and then an increase; if the increase is not well tolerated return to the smaller dose. The weight should be recorded weekly. The author's routine is to give one-tenth grain three times a day, with liquid paraffin or some other suitable laxative night and morning. A good working knowledge of the symptoms of slight thyroid insufficiency is essential, and it is certain that no drug gives more pleasure to both the patient and his medical advisor than thyroid gland given in the right dose to the right person.—M. B. G.

(THYROID) Intensive study of fifty cases of neurocirculatory asthenia. Friedlander (A.) and Freyhof (W. L.) Arch. Int. Med. (Chgo.), 1918, **22,** 693.

Of fifty cases of neurocirculatory asthenia studied, twenty per cent demonstrated to a greater or less degree, thyroid tumors. This is not considered unusual among men from the Ohio Valley region. Tremor was present in 96 per cent of the

cases. Little importance is attached to these findings as a possible factor in causation of neurocirculatory asthenia.
—H. W.

(THYROID) Les petits basedowiens (Minor exophthalmic goitre). Lian (C.) Presse Méd. (Paris) 1918, —, 665-67.

A general discussion tending to the conclusion that the "irritable heart of soldiers" is often due to minor degrees of exophthalmic goitre. This can be confirmed by the author's "hyperesthesia sign." (See "Le signe de l'hyperesthésie, etc." abstracted in this number of Endocrinology.)—R. G. H.

(THYROID) Le signe de l'hyperesthésie de la region thyroïdienne et le basedowisme fruste dans les troubles cardiaques des soldats (A sign of hyperesthesia in the region of the thyroid, and suspected exophthalmic goitre in cardiac disturbances of soldiers.) Lian (C.) Soc. Méd. des Hôp. de Paris, 1918, **42,** 1041.

In making systematic examinations of patients complaining of palpitation of the heart, Lian found in a certain number of instances, a hypersensitivity of the skin over the thyroid glands. This area of hypersensitivity may closely follow the margins of the glands, or may cover only parts of one or both lobes or the isthmus. In some cases the area of hyperirritability corresponds to the hypertrophied portions of the glands, hence the suggestion that the hyperirritability may mark out the location and extent of the diseased portion of the gland. In subjects suffering from circulatory or nervous disturbances simulating exophthalmic goitre, this sign of regional cutaneous hyperirritability may be the means of establishing the seat of the trouble directly or indirectly in the thyroid gland. It was noticed, however, that in chronic cases, where an enlargement had been of long standing, there might be no evidence of hyperirritability, consequently the sign is likely to be elicited only in the initial stages of thyroid abnormality or in its exacerbations.—A. L. T.

(THYROID LIVER) Hemophilia: Experimental data bearing on the effect of glycerinized extracts of visceral hemophilic tissue on the coagulation time of blood. Lowenburg (H.) and Rubenstone (A. I.) Arch. Ped., 1918, **35,** 757. Abstr. from J. A. M. A. Oct. 12, 1918.

The authors noted that normal tissue extracts uniformly accelerate the coagulation time of calcium plasma and that

most of the tissues of a hemophilic patient, with the exception of thyroid and liver, seem to exert almost the same influence on coagulation. Thyroid gland and liver not only caused a prolonged coagulation time, amounting to two and one-half times the corresponding normal time, but actually inhibited the action of the calcium added to the plasma, so that the coagulation of the calcium plasma was prolonged almost two minutes. These observations were repeated with uniform results and though admittedly limited to the tissues of one hemophilic, they are striking. There is a possibility that the thyroid and even the liver may secrete an antithrombic substance or enzyme, which may be in part, if not principally, the cause of the deranged coagulative mechanism of hemophilic blood.
—M. B. G.

(THYROID). Maladie de basedow et emotions de bombardements. (Basedow's disease and emotional states from bombardments.) Etienne (G.) et Richard (G.), Soc. Méd. des Hôp. de Paris, 1918, **42**, 1196.

Apropos the theories of Crile and of Cannon, regarding the intermediation of the adrenal glands in the etiology of Basedow's disease from psychic trauma, the authors describe two cases in which the views of Crile and Cannon appear to be confirmed; on the other hand two cases are reported resulting from comparable external causes, but instead of having an elevation of blood pressure there occurred a diminution. In the former two cases recovery was associated with a gradual fall of blood pressure to normal, while in the latter two cases the blood pressure rose to normal in the process of recovery. Consequently the assumption that the adrenal glands respond more readily to sympathetic nerve action than do the other endocrine glands owing to absence of intercalated neurones in the nerves passing to the adrenal glands does not form a safe basis for the generalization that hyper-activity of these glands is a precursor to dystrophy or abnormal functionation of the thyroid apparatus.

(It should also be noted that there is no unequivocal evidence that the adrenal glands have anything to do with the maintenance of vasomotor tone or general blood pressure.)—A. L. T.

(THYROID) Neues Verfahren zur Herstellung und Isolieren der inneren Sekretion der Schilddrüse, sowie auch der inneren Sekretion aller lebenden und überlebenden Drüsen und Organe (New method of isolating hormones). Eiger (M.) Zentr. f. Physiol. (Leipzig), 1917, **32**, 64-6, 209.

The method is to wash out the blood by saline fluid (Ringer's or Locke's) via the artery and then to continue the perfusion and collect the issuing fluid from the veins; the fluid will contain the natural secretion. The method has been applied to several endocrine and other organs and tissues, including tumors benign and malignant. Details are at present given only for the thyroid; its secretion is water-clear, and contains no protein, iodin, or choline. It keeps for months; it increases the action of small doses of adrenin and increases the output of phosphorus in metabolism experiments. Thyreoglandol (Roche) and Burrows and Welcome's tabloids used as controls have the same action in less degree.—Physiol. Abst., **3,** 328.

(THYROID) Note on the preparation of a soluble concentrated product of the thyroid gland. Rogoff (J. M.), Jour. Pharm. Exp. Ther. (Balt.), 1918, **12,** 207-9.

The preparation of a concentrated active product of the thyroid gland, which is soluble in water, is briefly described.
—L. G. K.

(THYROID) Observaciones experimentales sobre el exoftalmos hipertiroideo (Observations on experimental hyperthyroid exophthalmos). Marañón (G.) Congr. Asoc. Española para el Prog. de las Ciencias, Valladolid, Oct. 19, 1915.

Experimentally Marañón has been able to produce in rabbits the tetrad of symptoms characterizing Graves' disease, namely, emaciation, tachycardia, nervous excitability and light exophthalmos. The exophthalmos in thyroid-treated animals as in clinical Graves' disease was inconstant. If the animals were previously castrated the exophthalmos appeared more constantly and more intensely. Injections of glycerine extracts from a Graves' patient, herself not having exophthalmos, produced this symptom in a rabbit. This is a remarkable observation since the thyroid glands of such patients are usually depleted of active constituents. The symptom of exophthalmos was observed to be accentuated by fear in thyroid treated rabbits. In one such animal, which was literally frightened to death, the exophthalmos was very pronounced.—R. G. H.

(THYROID) Observations on the blood pressure in cases of dysthyroidism. Swan (J. N.) Interstate Med. J. (Chgo.), 1916, **23,** 186-203.

Discusses the varying degree of intensity of the blood pressure findings, in fifty cases of dysthyroidism. The observations were made during the operation of partial thyroidectomy, and at intervals for several weeks after operation. It was concluded that the first effect of dysthyroidism on blood pressure is to reduce it in the systolic phase. This is accompanied by disturbance of pulse pressure, usually, an increase. After a varying period the systolic pressure begins to rise and gradually chronic hypertension develops. Functional myocardial tests indicated that in nearly all cases the heart muscle was affected whether there were clinical symptoms of this or not.—R. G. H.

(THYROID) Observations on the prevalent types of GOITRE in western Washington. Jones (E. O.) Northwest Med. (Seattle), 1916, **15**, 13-16.

Jones cites the studies of D. C. Hall who found, among the students of the University of Washington coming from the counties on Puget Sound and on both slopes of the Cascade Mountains, goitre in 13 to 33⅓ per cent; while students from the eastern and southern counties of the state showed goitre in a very small per cent. The author accepts Plummer's classification and contrasts his own records of 150 cases with those of the Mayo Clinic. The chief differences were the relative infrequency of true exophthalmic goitres in Washington (16 per cent), and the proportionately large number of secondary hyperthyroidism (78 per cent). In 117 cases the average length of time between the appearance of the goitre and the onset of toxic symptoms was 6.3 years.—J. P. S.

(THYROID) Over hypothyreoide (Minor thyroid insufficiency). Bolten (G. C.) Psychiat. en neurol. Bl. (Amsterdam), 1918, **22**, 135-173.

In an excellent article B. points out that this condition plays a much more important role than even many endocrinologists believe. The following classification is offered:

A. Direct symptoms.
   1. Diminished gastro-intestinal secretions; nervous dyspepsia.
   2. Changes in metabolism; diminished oxidation; diminished salt excretion.
      a. Gout, sciatica, etc.
      b. Constitutional obesity.

c. Dercum's disease.

3. Symptoms of intoxication due to diminished production of enzymes.
   a. Nervous headache ("migraine").
   b. Epilepsy (genuine).
   c. Neurasthenia.
   d. Certain light cases of dementia precox.
   e. Symptoms of menopause.

B. Indirect symptoms due to sympathetic hypotonia.
   a. Atrophic diseases of skin, nails and subcutaneous tissue.
   b. Quincke's edema.
   c. Diminished power of regeneration of skin, bone, etc.

C. Mixed forms—myxedema (mixture of B and A, 3, d).

The possibility of endocrine factors in symptomatology should always be kept in mind.—J. K.

(THYROID, PARATHYROID) Eye affections following EXPERIMENTAL THYROIDECTOMY. Edmunds (W.) The Ophthalmoscope (London), 1916, **14,** 300-302.

Complete thyro-parathyroidectomy in dogs is frequently followed by cataract. Analysis of the experiments leads the author to conclude that the altered secretion of these organs produced by interference with their nerve supply is more inimical to the nutrition of the cornea than are the toxic effects due to their complete excision. Physiol. Abst., **1,** 245.

(THYROID) Postpneumonic strumitis. Zindel (L.) Beitr. z. Chir. (Tübingen) 1918, **110,** 649.

Description of a case of purulent inflammation of a goitre after pneumonia. Pneumococci were found in the pus in pure culture. Such cases are extremely rare. The author could find only 12 others in the literature.—J. K.

(THYROID) Preoperative considerations of exophthalmic goitre. Berkman (D. M.) St. Paul Med. J., 1916, **18,** 300-303.

A statistical analysis of the mortality records of the Mayo Clinic, 1914 and 1915. Among other things the data indicate that the duration of the disease prior to operation has little relation to the operative risk. Cardiac deterioration was relatively inconspicuous, but was present in some degree in all but 6 of the 24 cases reported. The operative mortality had reached

a level of 2.89 and 2.63 per cent, respectively, in the two years, a level which the author believes can not be much lowered without refusing operation to patients who should have the benefit of the doubt.—R. G. H.

THYROID preparations, A method for the standardization of—. Rogoff (J. M.) Jour. Pharm. & Exp. Therap. (Balt.), 1917, **10**, 199-208.

A method is described in which the specific action of thyroid gland (emaciation, angulation of head, etc.) upon tadpoles is used to assay the physiological value of commercial thyroid preparations. It was shown also that the value of thyroid is in proportion, not to its total iodine, but to the iodine in combination. (See Endocrin., 1917, **1**, 55-56.)—L. G. K.

(THYROID) Production of CONGENITAL GOITRE. McCarrison (R.) Proc. Roy. Soc. (Lond.), 1916, **89B**, 322-327; Indian J. Med. Res. (Calcutta), 1916, **4**, 183.

The experiments recorded were made on goats, and confirm the author's view that congenital goitre is due to the action on the fetal thyroid of toxic substances derived from the maternal intestine. These substances are the products of the micro-organisms originating in fecally contaminated soil which are conveyed to man and animals by infected food and water. The prevention (by muzzling, etc.) of the entry into the alimentary canal of anything but clean food and water prevents also the entry of the infecting agent. The goitres themselves were sterile. Physiol. Abst., **1**, 312.

THYROID, Report of a case of sarcoma of the—. Vanden Berg (H. J.) J. Michigan M. Soc. (Grand Rapids), 1917, **16**, 18-20.

A brief case report illustrated with photograph and two microphotographs. The case terminated fatally.—R. G. H.

(THYROID) Simple goitre. Cameron (M. H. V.) Can Med. Assn. J. (Toronto), 1919, **9**, 302-309.

A brief discussion of the classification, symptoms, etiology and treatment of goitre. Contains nothing new.—L. G. K.

(THYROID) Struma bij een meisje van 16 jaar (Goitre in a girl of 16). Noordenbos (W.) Nederl. Tijdschr. v. Geneesk. (Amsterdam), 1916, **60** (ii), 596.

A demonstration of a girl upon whom a goitre operation was performed. Histological examination showed cancer.
—J. K.

(THYROID) The effect of typhoid inoculation on endemic goitre at the Lawrence Military Asylum, Sanamar, Punjab. Nicholson (M. A.), Lancet (Lond.), 1916, (ii), 275-77.

This asylum was established in 1848, and after a few years endemic goitre became very common among its inmates. Nicholson found that inoculation against typhoid had no effect in any way on the course of the endemic goitre.—J. P. S.

THYROID. The etiology and treatment of exophthalmic goitre with special reference to the use of radium. Aikins (W. H. B.) Canada Lancet (Toronto), 1916, **49**, 548-59.

Data published elsewhere. See Endocrin., 1917, **1**, 104.

(THYROID) The effort syndrome together with a consideration of certain murmurs. Conn (A. E.) J. Am. M. Assn. (Chgo.), 1918, **71**, 2132-37.

Symptoms associated with exophthalmic goitre are in some respects like those found in the effort syndrome. The symptoms in common are nervousness, tremor and tachycardia. In the effort syndrome, exophthalmos or thyroid enlargement is usually absent. There need be no diarrhea. Tachycardia may be absent. The tremor is really no tremor, but a shake, and it attains degrees of severity never seen in the most advanced cases of exophthalmic goitre. On the other hand, when tachycardia in exophthalmic goitre develops to as high a rate as is attained in the effort syndrome, there is usually a certain degree of dyspnea as well, and the size of the heart is definitely increased, whereas there is no reason for believing that this occurs in the effort syndrome. Between the conditions, a striking difference is observed at night. When tachycardia and dyspnea in exophthalmic goitre are sufficiently severe to attract attention, they persist, as a rule. In the effort syndrome, on the other hand, both disappear. The presence of small thyroid tumors or slight symmetrical enlargement of the gland can scarcely be taken as evidence in favor of hyperthyroidism. Such enlargements occur in large numbers of persons in certain sections of the United States, as elsewhere. They are not necessarily accompanied by symptoms either of developing exophthalmic goitre or of the effort syndrome. (Quoted.)

(THYROID) The liberation of the internal secretion of the thyroid gland into the blood. Rogoff (J. M.) Jour. Pharm. Exp. Ther. (Balt.), 1918, **12,** 193-206.

An attempt was made to detect in the blood coming from the thyroid glands of three dogs, a physiologically active secretion, by feeding the dried blood to tadpoles. One dog, whose thyroid glands were rich in colloid and had a good iodine content, yielded evidence of an active secretion into the blood collected from the glands during massage and during stimulation of the cervical sympathetic nerve. This was not taken as evidence of the existence of secretory nerves to the thyroid since the slowing of the blood flow due to vasoconstriction during the nerve stimulation may have resulted in a higher concentration of the hormone in the blood coming from the gland, even though the rate of liberation remained constant. The other two dogs whose glands were hyperplastic and contained no detectable iodine yielded negative results.—L. G. K.

THYROID therapy in ophthalmic practice. Dunn (P.) Med. Press (Lond.), 1919, **107,** 200-202.

The author believes that the thyroid plays an important role in various diseases of the eye. Thyroid medication is valuable in "keratitis punctata" and in slowly healing corneal ulcers. The paper bears out a well grounded hypothesis that thyroid secretion is a potent general cell stimulant.—R. G. H.

(THYROID) The relative frequency in recruits with and without thyroid enlargement of certain signs and symptoms which occur in neurocirculatory asthenia. Addis (T.) and Kerr (W. J.) Arch. Int. Med. (Chgo.), 1919, **23,** 316.

From a survey of recruits, the authors found that those signs and symptoms which occur in neurocirculatory asthenia, and which may be present in toxic goitre were not more commonly seen in recruits with thyroid enlargement than in those who had no enlargement. The enlargement of the gland in such cases is considered incidental and not causative. The conclusion is drawn that the development of toxic goitre is not the cause of the syndrome even in men with thyroid enlargement. Hence, there is no reason why cases of thyroid enlargement with the syndrome of neurocirculatory asthenia should be considered as in any essential respect different from those without thyroid enlargement.—H. W.

(ULTIMOBRANCHIAL BODY) The origin of the ultimobranchial body and its relation to the fifth visceral pouch in birds. Johnson (C. E.) Jour. Morph. (Phila.), 1919, **31**, 461.

Observations on embryos of coot, gallinule, tern, and chick show that the true fifth visceral pouch in birds is a diverticulum distinct from that which gives origin to the ultimobranchial body. The last-named body, contrary to the usually accepted accounts, arises not from the fifth pouch, but from a diverticulum developed medially to the fifth pouch. Observations on embryos of the turtle, Chelydra serpentina, and comparisons with accounts based on other reptiles, show that the fifth pouch and the ultimobranchial diverticulum in birds are homologous with those of reptiles—Author's Abst.

VAGATONIA. Werley (G.) Southwestern Med. (El Paso, Tex.), 1918, **2**, 1-5.

A very brief case report with an uncritical exposition of Falta's well-known theories of autonomic pathology.—R. G. H.

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